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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

Vol. 39.] 1942. [No. 2.

SUMMARY OF RECENT ABSTRACTS.*

II. YELLOW FEVER.

Epidemiology: Animal reservoirs.

FINDLAY (p. 431) defines the yellow fever area in Africa, as shown by the mouse protection test. The limit is from the west coast at latitude 15°N., along the southern border of the Sahara to the Blue Nile, thence along the Sudan-Abyssinian border to western Uganda and along the Congo. There may, however, be foci in western Abyssinia.

In the *East African Medical Journal* (p. 432) there is mention of the epidemic of yellow fever which broke out towards the end of 1940 in the southern Sudan, and in which over 15,000 cases, with 1,600 deaths, were reported. There is strong evidence that the infection has long been present in the Sudan and that it is still present in every region where mouse protection tests have given positive results.

SICÉ and BROCHEN (p. 66) report three cases from the French Sudan. These occurred in jungle country from which cases have previously been reported, and this fact supports the view that there may be an animal reservoir in that region. SALEUN (p. 432) reports a few cases and a few positive protection tests, from French Equatorial Africa during 1939. One chimpanzee and one cow gave positive protection tests. CANTON (p. 65) gives an account of yellow fever in Dakar. Many of the outbreaks during the last 150 years are said to have originated in Sierra Leone and the Gambia, and in the most recent, in 1937, the disease was propagated along the Dakar-Niger railroad.

SMITH (p. 66) has found yellow fever immune bodies in the sera of 32 of 100 sheep, examined by the mouse protection test, from Kano, N. Nigeria. He inoculated sheep which had no protective bodies with suspensions of neurotropic yellow fever virus and in some instances symptoms similar to those caused by the rabies virus were produced. The virus survived for at least 13 days in the animals' brains, and sheep to sheep passage was effected; the animals developed immune bodies which gave protection to mice. The author concludes that the

* The information from which this series of summaries has been compiled is given in the abstracts made by the Sectional Editors in the *Tropical Diseases Bulletin*, 1941, Vol. 38. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

immune bodies found in sheep in Nigeria and Kenya probably develop as a result of acquired, and not natural, immunity, but it is not yet certain that infections other than yellow fever cannot produce them.

From British Guiana SNEATH (p. 67) reports that recent protection tests on human sera show that certain areas are more important than others as foci of the disease, and that, since some of the positive sera were found in children, yellow fever is endemic in the hinterland.

DE ASSUMPÇÃO (p. 433) reports that with the protection test in which the material was inoculated intraperitoneally into the Brazilian house rat (camondongo), positive results were obtained in 56·8 per cent. of 139 persons from areas of the State of São Paulo, in which there was an epidemic of jungle yellow fever in 1937–38. Most of the sera were from patients who had had the disease or who were suspected of having had it. DA FONSECA (p. 66) found that the blood of the monkey *Alouatta fusca* (the red howler monkey), after infection with the Asibi strain of yellow fever virus, was infective for Swiss mice during the period 8–14 days after the infection, but that no symptoms or signs of the disease could be found in the monkey during life or at autopsy. DA FONSECA and ARTIGAS (p. 67) found the monkey *Cebus cirrifer*, in Botacatú, São Paulo, to be susceptible to infection with the Asibi strain. The monkeys responded with pyrexia, but did not die, and the virus could be isolated from the blood on the fourth but not on the ninth day.

BUGHER *et al.* (p. 434) have tested the susceptibility to yellow fever of marsupials in eastern Colombia. Multiplication of the virus in the blood produced no obvious signs of illness in any, but circulating virus was found, between the fourth and ninth days after infection, in 17 per cent. of the animals. Protection tests were positive in 23 per cent. ; antibodies are not usually transmitted by mothers to offspring through the placenta or the milk. Results obtained in *Didelphys marsupialis* captured during and after an outbreak of jungle yellow fever indicate that these animals must play some part in the epidemiology of the disease.

BUGHER (p. 434), in giving an account of the methods used and precautions taken in the examination of sera of wild animals in Colombia, makes the point that animals in which the virus may circulate without causing illness, and which are therefore free to roam, constitute a greater danger to man and other animals than those which are rendered seriously ill or are killed by the disease. He defines a susceptible animal as one in which the virus can multiply, irrespective of its effect on the host. In discussing the mouse protection tests he points out that variation in the susceptibility of the strains of mice employed is a factor to be taken into account, and that calculation of the amount of virus to be used can only be made after desiccation. In control tests, a pool of known immune serum is used, but it was found that after being kept for almost two years, such a pool showed a definite decline in antibody titre.

Antibody activity, sufficient to protect half the mice used, was found in a pool of human serum from persons thought to be non-immune, and it was found that certain animals showed definite non-specific anti-virus activities. Of these the domestic pig and the peccary are examples, but they are susceptible to infection with the virus ; in protection tests, therefore, larger doses of virus are needed for these animals than for others. The buzzard also shows anti-virus properties.

The same author (p. 437) finds that Swiss mice less than nine days old are as susceptible to subcutaneous injection of yellow fever virus as adult mice are to intracerebral inoculation, when both neurotropic and viscerotropic strains are used, but that the difference in incubation period between the neurotropic and viscerotropic strains is not shown when the subcutaneous route is used in the young mice. In transmission experiments it was observed that infected *Aëdes aegypti* could infect these young mice by bite even when the mosquitoes did not, so far as could be seen, withdraw any blood.

Aetiology: Transmission.

Pickels and Bauer (p. 69) give the results of a study of the physical properties of the yellow fever virus.

Findlay and MacCallum (p. 68) report on attempts to grow the attenuated viscerotropic strain of yellow fever virus, known as 17 D, in a variety of media. Success was only achieved in Tyrode media containing certain living tissue cells: fowl or mouse embryonic tissue, human placental tissue or the tissue of mouse carcinoma or sarcoma, but no growth occurred with adult mouse brain tissue, or that of larval *Aëdes aegypti*, nor with fowl embryo cells heated to 56°C. for 30 minutes, nor in media lacking living cells but containing amino acids or digested cells. Living *Bact. coli* or yeast cells failed to support growth. The virus grew in the absence of serum and glucose. The authors suggest that viruses possess few or no enzymes of their own, and are forced to borrow enzyme systems from the living cells they parasitize. The same authors (p. 68) have found that the passage of 8–10 bubbles of oxygen each minute through the culture media permits the use of at least 30 cc. of medium in place of the usual 5 cc., and thus reduces the labour involved in the growth of large quantities of the virus. No change in the pathogenicity of strain 17 D has been found by this method, and the titre is maintained. The same procedure is successful with certain other viruses.

Fox and Gard (p. 69) show that the duration of activity of dried yellow fever virus is inversely proportional to its residual moisture content. With storage in air at 4°C. the critical moisture content is between 4 and 5 per cent. Keeping qualities are improved, below this critical moisture content, if the material is sealed in nitrogen or in a vacuum. These results suggest that the inactivation of the virus is, at least in part, the result of an oxidation reaction.

Findlay (p. 431) states that the only mosquito found infected in nature in Africa is *Aëdes aegypti*, though several others, the names of which are given, may transmit the disease by bite in the laboratory. Only in the region of Malakal in the southern Sudan is there epidemiological evidence to suggest that *Taeniorhynchus* (*Mansonioides*) *africanus* may act as a vector.

Control.

For the control of yellow fever in East Africa a conference held in Nairobi (p. 432) considered that it was of paramount importance to eliminate *Aëdes aegypti* from all seaports, steamships and dhows on the coast and on lakes Victoria and Tanganyika, and from all inland towns, aerodromes and premises near railways. Certificates of immunity or of non-exposure should be required of all travellers from infected

areas, and all persons likely to travel by air in Africa should be vaccinated. Le Van (p. 70) gives an account of measures to control *Aëdes aegypti* in Florida. Repeated painstaking house inspections must be made to eliminate all possible breeding places in artificial containers; Gambusia is useful in dark drinking water cisterns, the fish being first kept overnight in water chlorinated to 0·1–0·15 parts per million residual chlorine. The spraying of houses with pyrethrum extract in oil is employed, and breeding is controlled in piles of old motor car tyres by spraying with Paris green, and in cemetery vases by pellets of Paris green. It is noted that eggs of *Aëdes aegypti* laid in wooden egg troughs remained viable for one year, during which period there had been no frost.

Napier (p. 437) gives an account of the precautions taken to prevent the entry of yellow fever into India. These follow the usual lines and include a quarantine period of nine days, which must elapse before air passengers from infected areas are allowed freedom. In no circumstances is virus allowed to be imported, even by laboratory workers.

Canton (p. 65) describes the organization of the public health service in Dakar as regards prevention of yellow fever, and mentions the method of vacccination simultaneously against yellow fever and smallpox. Smith *et al.* (p. 70) report that in Colombia, from 1937 to 1940, 175,496 persons were vaccinated with virus 17D. Of 2,139 examined up to two years after vaccination, almost 90 per cent. were found to be immune. *Charles Wilcocks.*

YELLOW FEVER.

Rockefeller Foundation. A Review for 1940 [Fosdick (Raymond B.), President]. pp. 27–31. With 2 figs.—**Unraveling the Yellow Fever Mystery.**

In this brief note a reference is made to the recent outbreak of yellow fever in the Nuba mountains of the Sudan which, it is stated, was probably transmitted by *Aëdes aegypti*, although there is a bare possibility that other vectors were involved [see below].

In recent work on jungle yellow fever in South America it has been shown that in wild animals inoculated with the virus no illness is as a rule produced, but the virus is present in the circulating blood while the animals are running about, a condition especially favourable to the spread of the virus. Several groups of animals are susceptible, the chief of which are :—

Primates : man and monkeys.
Marsupials : the opossums, all species.
Edentates : anteaters, sloths, armadillos.
Rodents : agouti, paca, capybara, some species of mice.
Certain generalizations are made :—

" 1. Yellow fever is primarily a disease of jungle animals. The classical form involving transmission from man to man by the *Aedes aegypti* mosquito is more of a secondary cycle depending largely upon conditions of population concentration and mosquito breeding created by man himself.

" 2. Transmission of jungle yellow fever appears to be by jungle mosquitoes from animal to animal.

" 3. There is no animal reservoir of virus in the usual sense. Virus continues to circulate in the blood of susceptible animals for three or four days only, and does not subsequently reappear. Mosquitoes, however, once infected tend to harbour the virus for the remainder of their lives, which may be several months under favorable conditions."

In jungle yellow fever vaccination is the most important control measure, but it is pointed out that the great value of control of *Aëdes aegypti* in urban areas has been in no way diminished, and that if this mosquito were controlled in towns the risk of transmission of the disease to East Africa, India and the Orient, in these days of fast travel, could be avoided. *C. W.*

FINDLAY (G. M.). **The First Recognized Epidemic of Yellow Fever.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1941. Nov. 29. Vol. 35, No. 3. pp. 143–154. [27 refs.]

FINDLAY (G. M.). **The Present Position of Yellow Fever in Africa.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1941. Sept. 9. Vol. 35, No. 2. pp. 51–72. With 2 maps. [18 refs.] Discussion pp. 72–76 [SMITH (Hugh H.), MACKIE (F. P.), GILL (G. A.), STANNUS (H. S.), RICHARDSON (D. T.), MENZIES (T.), HEWER (T. F.) & FINDLAY (G. M.)].

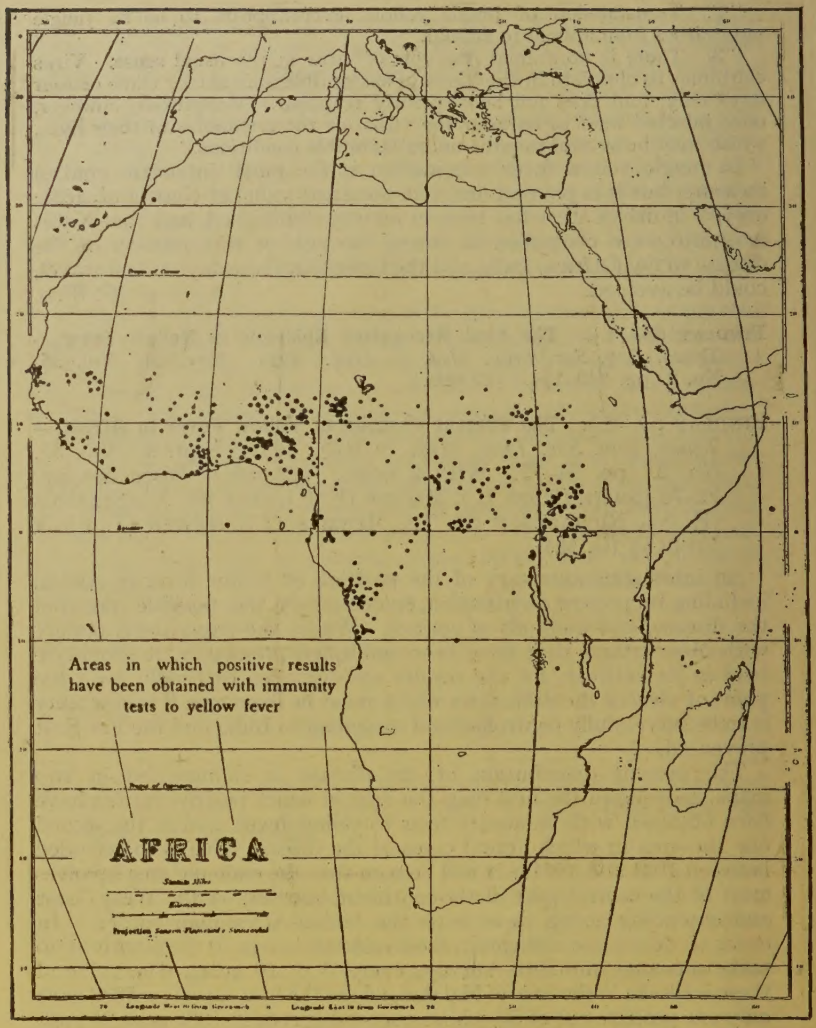
An interesting summary of the position of yellow fever in Africa, including its present distribution, epidemiology, the possible spread of the disease, and methods of control. Whilst the paper deals mainly with observations that have been published previously, it should be read in its entirety, for the results are discussed especially from the point of view of the difficulties which must be overcome if yellow fever is to be successfully controlled and its spread to India and the Far East prevented.

The present distribution of the disease is summarized in two maps, showing in the first map the area in which positive results have been obtained with immunity tests to yellow fever, and in the second one the area in which actual cases of the disease have been recorded between 1921 and 1941. It will be seen that the endemic area involves most of the central part of the continent, starting on the West Coast and extending across to at least the Sudan-Abyssinian border. In order to determine changes in these endemic zones, it is important to make repeated immunity surveys every 5 or 10 years. The value of these is shown in the case of Malakal, where the first survey in 1933 gave only one positive out of 50, whilst a second survey in 1938 gave 21 positive out of 114. The most peculiar feature of the distribution of yellow fever is the occurrence of isolated cases without any apparent relationship to epidemics. In Freetown, where no case had occurred since 1910, a single European official died of yellow fever in 1935, and no other cases could be found in the neighbourhood.

As in South America, it is possible to distinguish three epidemiological types of yellow fever, showing respectively urban epidemicity, rural epidemicity and rural endemicity.

Typical urban outbreaks occcurred in Lagos in 1925–26, in Bathurst in 1934–35, in Accra in 1926–27 and again in 1937. In all these outbreaks *Aëdes aegypti* would seem to be the sole vector.

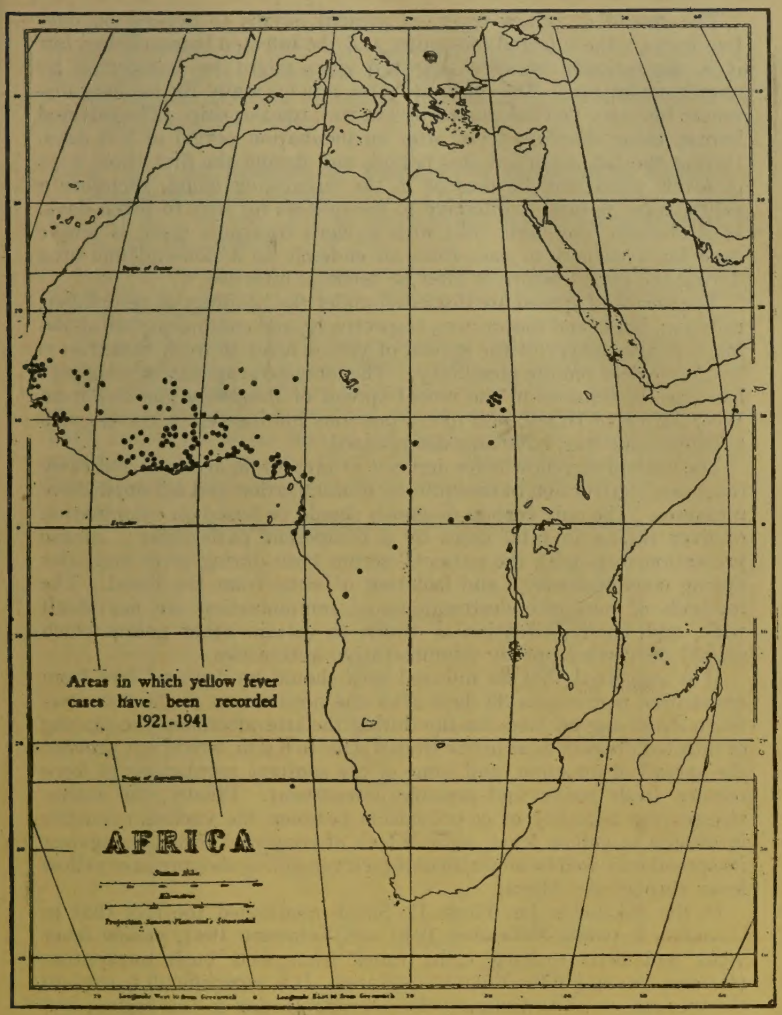
The most striking rural epidemic ever recorded in Africa is that which has recently occurred in the Anglo-Egyptian Sudan [see below p. 69].



[Reproduced from the *Transactions of the Royal Society of Tropical Medicine and Hygiene.*]

Smaller epidemics have been recorded from Ashanti in 1933, and in certain isolated villages of the Gold Coast in 1937. In none of these epidemics were infected *A. aegypti* caught in association with actual yellow fever cases, although this mosquito is widely distributed and breeds readily in the water in hollow trees, etc. Whilst at present it is impossible to exclude *A. aegypti* as a vector in these rural epidemics it is possible that other species of mosquitoes may play an accessory rôle.

Endemic yellow fever may be carried on entirely by the mosquito-man cycle, but hitherto efforts to isolate virus from patients with febrile symptoms in areas with a low rate of endemicity have not been successful.



[Reproduced from the *Transactions of the Royal Society of Tropical Medicine and Hygiene.*]

It is possible that the virus may be carried on by a mosquito-animal cycle, and there is considerable evidence to show that many wild and domestic animals may serve as hosts. Tables are given summarizing the results of applying the mouse protection test to the blood of African primates, domestic animals, and birds, many of which contain virucidal properties. It is also possible that the virus may persist for long periods in some other species of vertebrate or invertebrate, and it is known that the disease can persist for some months in the absence of infected mosquitoes.

The spread of yellow fever, at present, seems to depend on only two factors, the infected mosquito, and the infected human being, but it is theoretically possible that the virus might be transferred by migratory animals. The mosquito does not normally fly for long distances but may be transported by air, rail, road or ship. The infected human being develops fever after an incubation period of 2–6 days. During the latter part of this period, and during the first three days of fever, virus may be present in the circulating blood, therefore a yellow fever patient is infective to mosquitoes for four to seven days. It is obvious, therefore, that with modern transport there is ample time for a patient to pass from an endemic to a non-endemic area during the period before or after he becomes infective.

The means of spread are discussed under the headings of aeroplanes, railways, boats and motor cars, respectively, and examples given showing that the danger of the spread of yellow fever to fresh countries is by no means a remote possibility. The increased rapidity of transport has already resulted in the recent spread of *Anopheles gambiae* from West Africa to Brazil, and many previous hindrances to travel, such as internecine war, have now disappeared.

The control of yellow fever depends at present on accurate and early diagnosis, destruction of mosquitoes, immunization and administrative measures. The only certain diagnosis should be based on examination of liver tissues in fatal cases by a competent pathologist; mouse protection tests with the patients' serum both during fever and later during convalescence; and isolation of virus from the blood. The methods of mosquito destruction and immunization are next dealt with, and, finally, attention is drawn to certain other points which should be carried out by administrative authorities.

It is suggested that an infected area should be declared free from quarantine restrictions 30 days after the notification of the last case. Since *Aëdes aegypti* bites readily during the late afternoon the placing of infected areas in quarantine from 6 p.m. to 6 a.m. would not prevent the spread of infection, and some of the sanitary regulations in force require fresh study and possible amendment. Finally, the author stresses the necessity of co-ordination between the various countries interested in yellow fever, since a lack of concerted measures against its spread may well be an important factor in aiding the spread of yellow fever throughout Africa.

In the discussion Dr. Hugh H. Smith mentioned the fact that in Colombia between November 1940 and February 1941, yellow fever virus had been isolated eight times from wild bush mosquitoes (*Haemagogus* sp.) in the Villavicencio area. It is very difficult to explain the mechanism of continuing yellow fever infection in this region, and hitherto there is no agreement among the various workers in South America as to whether yellow fever infection remains in particular endemic areas for long periods of time, or whether the infection travels through the bush and returns to a given area periodically.

E. Hindle.

FINDLAY (G. M.). **Yellow Fever and the Anglo-Egyptian Sudan: Historical.**—*Ann. Trop. Med. & Parasit.* 1941. Oct. 21. Vol. 35. No. 1. pp. 59–65. [16 refs.]

"Although there is no definite account of an epidemic of yellow fever in the Anglo-Egyptian Sudan in historic times, natives of Kordofan

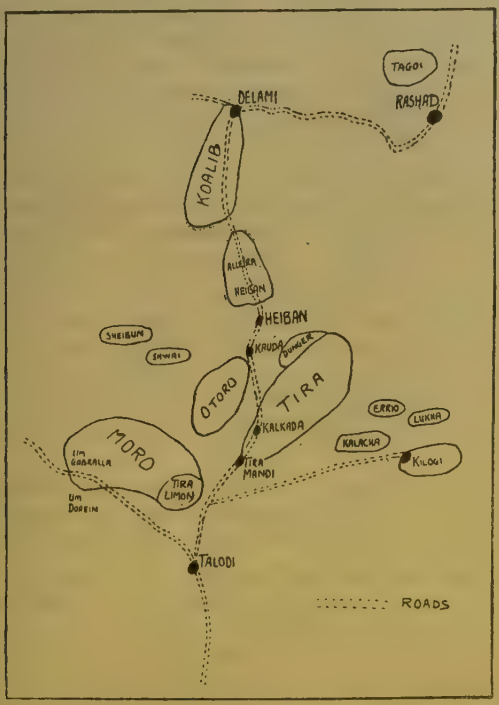
were immune to yellow fever when taken to Mexico in 1863. There is also evidence that they were far more resistant than Egyptians to fevers present in the Upper Nile Province of the Anglo-Egyptian Sudan.

"There is no evidence to suggest that yellow fever has been recently introduced into the Sudan."

KIRK (R.). **An Epidemic of Yellow Fever in the Nuba Mountains, Anglo-Egyptian Sudan.**—*Ann. Trop. Med. & Parasit.* 1941. Oct. 21. Vol. 35. No. 1. pp. 67–112. With 2 maps, 9 charts, & 4 figs. on 2 plates. [30 refs.]

A detailed account of a most important outbreak of yellow fever in the Nuba Mountains, the most striking rural epidemic of the disease ever recorded from Africa.

The possible existence of yellow fever in this district had previously been brought to notice by the discovery that a considerable percentage of the natives gave positive mouse protection tests, but no evidence of a disease clinically resembling yellow fever could be obtained. In 1940, during the latter part of the rainy season, an obscure epidemic appeared in the Tira and Otoro hills. The author, two British colleagues and a Sudanese laboratory assistant, with servants, went to



Sketch-map of the yellow fever epidemic area in the Nuba Mountains, showing the affected hill-groups.

[Reproduced from the *Annals of Tropical Medicine and Parasitology*.]

this district and, being non-immunes, most of the original party went down with the disease, which was proved beyond any doubt to be yellow fever.

A description of the country, climate and population is followed by a brief account of the wild mammals. The fauna includes monkeys and Pruner's hedgehog, both susceptible to yellow fever; local enquiries, however, failed to produce any indication of an epizootic among the hedgehogs.

The course of the epidemic is rather difficult to trace but it probably originated in Tira Limon, where cases occurred in May 1940. This is one of the highest and most inaccessible hills of the Moro group and is inhabited by the wildest of all the Nuba tribes. The way in which it spread in the Moro block, until after mid-July it extended to other parts of the Nuba Mountains, is discussed. The epidemic died out towards the end of November, the last cases occurring in Tira, Otoro and Alleira. It is curious that the disease inspired great dread among the people, although there was only a short illness with comparatively low mortality.

A clinical diagnosis of yellow fever seemed to be justified by the main features of the epidemic, a short, influenza-like fever, associated with cases of jaundice, and deaths preceded by " black vomit," occurring in an area with positive mouse protection tests. The diagnosis was confirmed by examination of the livers of fatal cases, by the demonstration that yellow fever immune bodies developed in the blood during the course of the disease, by the isolation of typical yellow fever virus from the blood of patients during the early febrile stages, and finally, by the results of epidemiological studies, which showed that the epidemic was followed by a rise in the proportion of immunes in the population.

The cause of the epidemic cannot be defined with any certainty, but owing to the war, conditions in the Sudan generally were unusually favourable to the spread of the disease, since large numbers of non-immunes were introduced. There is no evidence, however, that the war was responsible for initiation of the outbreak, for the Nuba Mountains lie off the main routes of communication. There is evidence in support of the view that the virus has been present there for a very long time and certainly in the recent past, but the reason for the sudden development of an epidemic of this magnitude is very difficult to explain. The results of immunity surveys, made in 28 places in the area before the epidemic, show that 22 contained positive sera in percentages ranging from 7 to 80 per cent., with 3 as the age of the youngest positive donor.

The incidence and mortality are summarized in the table below.

The disease attacked both sexes and all ages with no discrimination in respect of race, physical condition or social status, but very young children seemed to escape.

The mortality rate was approximately 10 per cent., but the true rate is probably much lower since there is good evidence that many mild cases were not recognized.

The general course of the disease is described from records of over 300 cases observed personally by the author. The onset was generally sudden, with fever, severe headache, pains in the neck, loins and legs, often with vomiting. There was congestion of the eyes, without coryza. Albuminuria was present, increasing in amount as the disease progressed. The tongue was small and pointed, furred in the centre, but

Yellow Fever: incidence of cases and deaths in the Nuba Mountains, 1940.

Locality.	Population.	Cases.	Deaths.
Tira Limon	6,000	—	—
Moro	20,000	4,970	548
Otoro	17,000	4,718	476
Tira	9,000	3,726	328
Shwai	3,000	302	30
Heiban	11,000	364	89
Koalib	22,000	64	4
Kilogi	7,000	788	65
Sheibun	2,000	330	35
Talodi	12,500	5	2
Total	—	15,267	1,577

clean at the edges and tip. The influenza-like fever might last anything from a few hours to three or four days, after which complete recovery might occur; or else more severe symptoms appeared, such as slowing of the pulse, jaundice, haemorrhages from gums, nose or stomach, "black vomit," melaena, and reduction or suppression of urine. The illness was always short, the patient being either dead or out of danger inside a week. When death occurred it was usually between the fourth and sixth day.

Convalescence was not usually rapid, the decline in fever being followed by a variable period of very marked asthenia in all except the very mildest cases. The only serious complication observed was myocarditis which caused a number of late deaths.

The development of *immunity* was tested by making mouse protection tests with blood samples of the patients collected at the beginning of the fever and a few days later. The results indicate that demonstrable immunity appears suddenly about the fifth day of the disease.

A post-epidemic survey was carried out in January 1941, shortly after the epidemic had subsided, and in one district the percentage of immunes had risen from 1 in 15 to 13 in 15 tested. The results for three districts are summarized in the following table :—

Comparison of the number of recorded cases in Heiban, Otoro and Tira with the number estimated from immunity surveys.

	Heiban.	Otoro.	Tira.	Total.
Population	11,000	17,000	9,000	—
No. of cases recorded ...	364	4,718	3,726	8,808
Percentage	33	28	41	—
Percentage of immunes in pre-epidemic surveys ...	10[4 in 41]	—[0 in 8]	7[1 in 15]	—
Percentage of immunes in post-epidemic surveys	63[26 in 41]	63[5 in 8]	87[13 in 15]	—
Percentage of population immunized during epidemic	53	63	80	—
Estimated no. of persons immunized during epidemic	5,830	10,710	7,200	23,710

[The numbers of sera examined were small; it is perhaps unwise to base estimations of large numbers on these percentages, though no doubt the author's main conclusions are justified.]

The chief interest of this epidemic lies in the number of mild cases which were recorded, and the author gives examples showing some of the difficulties encountered in their diagnosis. Many of the early cases were overlooked at the beginning, and if more severe cases had not occurred, the epidemic might have been regarded as influenza, sandfly fever, or one of the other "three-day fevers" encountered in the tropics.

Liver specimens were obtained by viscerotomy from seven fatal cases and all showed typical pathological changes.

With regard to the vector it is unfortunate that only incomplete entomological data are available, but it can be stated definitely that *Aëdes aegypti* was present throughout the epidemic area. Although essentially a domestic species, it has been found breeding in the Nuba mountains 2–3 miles from the nearest house. In addition to *Aëdes aegypti*, other species, able to transmit yellow fever in the laboratory, were found in the affected area, especially *Aëdes vittatus*, which is very abundant during the rains, breeding in rock-pools near the hills.

E. H.

League of Nations. Health Organisation. Eastern Bureau, Singapore. Annual Report for 1940. pp. 71–76. With 1 map.—**Yellow Fever.**

Yellow fever broke out in the Nuba mountains of the Sudan soon after the July–August rains of 1940. The infected country is entirely mountainous, and Aëdes mosquitoes are prevalent in small numbers during the rainy season, breeding in tree holes and domestic water collections. There has been a widespread infection with the virus for the past 20 years, but clinical cases were not found until this outbreak occurred. The outbreak is stated not to have been introduced from West Africa, as the affected area is far removed from all lines of communication. It appears, therefore, that the disease has been lying dormant in this area for several years and has now flared up in virulent form.

The steps taken by the Sudan Government included the following:—

"(*a*) Declaration of the area as infected with yellow fever from 7th November;
"(*b*) Strict isolation of the area and restriction of movements of persons;
"(*c*) Egress was only permitted when essential, and then after a quarantine period of ten days at the control posts;
"(*d*) The whole area was closed to air traffic and the aerodromes of El Obeid and Juba were declared anti-amaryl;
"(*e*) Intensification of anti-aedes measures; and
"(*f*) Further investigation by specialists."

Reference is made to the work of Whitfield, who has found the following species, known to be capable of carrying yellow fever in the laboratory or in nature, among the insects collected in aircraft at the aerodromes of the Sudan:—*Aëdes aegypti*, *A. luteocephalus*, *A. simpsoni* and *Mansonia africana*. But the comparative absence of *Aëdes aegypti* in the Nuba mountains has led to the suspicion that this outbreak may be due to the jungle type of the disease. Investigations on this point are in progress.

C. W.

GAST GALVIS (Augusto). Resultados del examen de las primeras 5,000 muestras de higado humano obtenidas en Colombia para el estudio de la fiebre amarilla. [**Results of the Examination of the First 5,000 Liver Specimens Obtained in Colombia for the Study of Yellow Fever.**]—Reprinted from *Rev. de Hig.* Bogota. 1941. Apr. No. 4. 29 pp. With 4 graphs. [15 refs.]

In 1930, the Yellow Fever Service of Brazil, searching for a method to discover outbreaks of the disease in isolated communities where its presence was otherwise not suspected, developed an instrument known as the viscerotome. An extensive service was set up which made possible the routine collection of liver specimens from rapidly fatal febrile cases by non-medical personnel over wide areas, with a minimum of expense and trouble [see this *Bulletin*, 1934, Vol. 31, p. 836, and 1937, Vol. 34, p. 686]. In 1934, shortly after jungle yellow fever had been shown to exist in the interior of Colombia, it was decided to introduce viscerotomy into that country as a routine procedure of the yellow fever service then being organized by the National Department of Health in co-operation with the Rockefeller Foundation. This report sets forth the results obtained in the examination of the 5,000 specimens of human liver collected by the viscerotomy service in Colombia between September 1934 and February 1940. During this period 117 viscerotomy posts were established throughout the country in carefully selected localities where climatic conditions made it seem likely that yellow fever might appear. The representative in charge of each post was directed to obtain a piece of liver from each individual in his area who died from any acute febrile illness of not more than ten days' duration. These specimens, preserved in formalin, are sent by post to the central laboratory for examination. Thus over this period of years there has been established a routine service, which functions most satisfactorily, for the rapid detection of yellow fever outbreaks in widely separated and isolated places.

Among the 5,000 liver specimens examined were 196 diagnosed as being positive for yellow fever. In many of these cases the diagnosis was confirmed by subsequent field investigations. By means of this service it has been possible not only to prove the presence of yellow fever in several regions of Colombia in which it was not previously suspected, but also to demonstrate that it does not exist in many other parts of the country where the conditions are apparently favourable for its propagation.

Although the chief function of the viscerotomy service is to find yellow fever, it is also of value in the discovery of various other diseases which produce characteristic liver lesions [see this *Bulletin*, 1935, Vol. 32, pp. 126–127 and 481]. Epidemics of fatal malaria and areas of high malarial endemicity are quickly brought to light. An interesting series of cases showing acute massive liver necrosis is reported from two widely separated districts of Colombia. Such cases are known to have been occurring in these same regions for many years and were formerly confused with yellow fever. The aetiology is still unknown. *Hugh H. Smith.*

VAN SOMEREN (E. C. C.). **Yellow Fever Control. Key and Chart to the Known Aedes Adults of Kenya.**—3 pp. With 14 figs.

Appended to this key is a series of figures showing very clearly the thoracic markings of 14 species. *C. W.*

ROZEBOOM (L. E.). **The Overwintering of *Aëdes aegypti* L. in Stillwater, Oklahoma.**—*Proc. Okla. Acad. Sci.*, Norman, Okla. 1939. Vol. 19. pp. 81–82. [Summarized in *Rev. Applied Entom.* Ser. B. 1941. Aug. Vol. 29. Pt. 8. p. 128.]

"It is shown from a brief review of the literature that the range of *Aëdes aegypti*, L., may be divided into a permanent region, where the temperatures are high enough for it to breed continuously, a border-line zone, where it hibernates in the egg stage, and a temporary summer region into which it may spread during warm weather but in which it does not survive the winter. The extent of this summer region is evidenced by the epidemics of yellow fever that occurred as far north as Philadelphia, New York and Boston before the method of controlling the disease was known.

"*A. aegypti* seems to be fairly common in Oklahoma and becomes an annoying household pest in Stillwater during the latter part of the summer. As Stillwater is not far from its northern limit of permanent distribution, a laboratory colony was established from adults collected locally in 1937, and three batches of eggs from it were exposed to winter conditions to find if they would survive. They were kept throughout the winter on sand in wide-necked bottles; two in one bottle were in a shed where they had some protection from snow and rain but none from cold; the other bottle was placed on the ground outside. The eggs were brought into the laboratory and immersed in water in April. Only one larva hatched from the batch of eggs that had been kept outdoors and it died in the pupal stage, but large numbers hatched from the other two batches and developed into vigorous adults. During the winter there were several periods when the temperature dropped considerably below freezing point for 4–9 days in succession; on the coldest day the maximum was 32°F. and the minimum 8°. The distribution of the mosquito at Stillwater in the summer of 1938 suggested that many eggs had survived the winter in nature. An unusually severe winter might possibly destroy all eggs exposed to it, but since the mosquito breeds in and around houses and barns, the protection thus afforded would probably be sufficient to ensure its permanent existence."

VILLELA (Eudoro). **Histology of Human Yellow Fever when Death is Delayed.**—*Arch. Pathology.* 1941. June. Vol. 31. No. 6. pp. 665–669. With 1 coloured plate.

Death from yellow fever usually occurs within 10 days of the onset. A number of workers have established criteria for the histological diagnosis of such cases. The chief changes in human livers are:—a salt and pepper distribution throughout the entire lobule, with greatest prevalence in the midzone, of rounded refractile acidophilic bodies, the so-called Councilman bodies. These acidophilic bodies sometimes show the "shadows" of nuclei within them: they are the remains of parenchymatous cells that have undergone a specific type of necrosis.

An absence of complete necrosis of the central zone of the liver lobule. A few non-necrotic cells can always be found among the cells immediately adjacent to the central veins even though at first sight all the cells seem to have undergone the acidophilic change.

A jumbling of the trabeculae, more accentuated in the mid-zone of the lobule than elsewhere.

Fatty degeneration of varying intensity generally more abundant in the centre and periphery than in the mid-zone of the lobule.

Findings of secondary value in the diagnosis of acute cases include nuclear changes such as oedema and intranuclear inclusions: the latter have not proved of practical value in the routine examination of material collected by viscerotomy in South America and fixed in 10 per cent. formaldehyde in physiological saline. [Intranuclear inclusions are not well preserved by this fixative: Zenker's fluid is preferable. In most human livers only 20 to 30 per cent. of parenchymatous cells exhibit intranuclear inclusions, but in some African outbreaks, *e.g.* Accra in 1937, nearly 70 per cent. of the liver cells showed them.] Other changes are varying leucocytic infiltration, principally of mononuclear cells, most pronounced in the mid-zone; yellow pigment inside the parenchymatous cells of the central zone; hyperaemia of the sinusoids, especially in the mid-zonal region.

In the case of a patient who had died on the 17th day after the onset of illness a clinical diagnosis of yellow fever had been made because of the classical symptoms and of other cases, on the same fasenda, in which the typical liver changes were noted. In the liver of this case the most prominent finding was of bright ochre-coloured granules scattered among a few Councilman bodies. An examination of other livers, more especially from cases where death had occurred on or after the eighth day, showed a varying number of these ochre bodies. These ochre bodies vary in size but are generally smaller than Councilman bodies. They may be free among the non-necrotic parenchymatous cells or more often within macrophages and Kupffer cells. In unstained frozen sections they are dirty-yellow or ochre-coloured; they remain unchanged after treatment with acid alcohol or hydrogen peroxide; are coloured orange ochre with Sudan III; are black in material stained by the del Rio Hortega method (impregnation with silver carbonate, counterstaining with gold chloride), the Councilman bodies being dark violet; and are negative to the Prussian blue test for iron.

In some livers where Councilman lesions are absent or so few in number as to make a diagnosis of yellow fever difficult, the ochre-coloured granular bodies show a distribution exactly similar to that of Councilman bodies in classic yellow fever. By examining a number of preparations it has been possible to follow the transition in colour from the eosinophilic pink of the early Councilman lesions through brownish yellow to the bright ochre of the granular bodies, which must be regarded as the last stage of the Councilman lesion, probably after impregnation with bile pigments.

The presence of the ochre bodies can be used as a basis for the diagnosis of yellow fever provided the following suggestive changes are also found—fatty degeneration, usually slight in degree and most frequently in the central zone; slight jumbling of the trabeculae in the mid-zone; increase in size of the nuclei of the parenchymatous cells; hyperplasia of the Kupffer cells, and the presence of leucocytes, most frequently in the mid-zone.

As a result of the finding of these ochre bodies in the liver every specimen of liver which had a histological diagnosis at variance with the clinical diagnosis was re-examined, and on the basis of the presence of the ochre bodies a diagnosis of yellow fever was established in 23 in which death had occurred 8 to 17 days after the onset of illness. From one of these cases yellow fever virus had been isolated from the blood on the second day of illness. *G. M. Findlay.*

DUFF (D.). **Diagnosis of Yellow Fever.** [Correspondence.]—*Brit. Med. Jl.* 1941. Sept. 6. p. 357.

The writer of this letter remarks that in the early days of outbreaks of yellow fever in the Gold Coast the cases are often missed, and points out that experienced medical officers place considerable reliance upon frequent examination of urine to detect the marked increase in albumin which occurs from the second or third day onwards. A diagnosis is usually made in the presence of the following group of symptoms: Sudden pyrexia, early prostration, severe frontal headache with congestion of the eyes, backache and increasing albuminuria. Jaundice and haemorrhages are later symptoms, and in mild cases jaundice may hardly be noticeable.

There is no quick test for the disease in the early stages, but the occurrence of cases with the foregoing syndrome in an endemic area justifies prompt application of local preventive measures.

In treatment it is vitally necessary to withhold all food in the early days of the illness—ingestion may be followed rapidly by a profuse haematemesis and death. *C. W.*

UGANDA PROTECTORATE. ANNUAL REPORT OF THE MEDICAL DEPARTMENT FOR THE YEAR ENDED 31ST DECEMBER, 1940 [SHELTON (C. F.), Ag. Director]. Appendix I. pp. 14–15.—**Summary of the Main Conclusions and Recommendations of the Conference held at Nairobi in December, 1940, for the Control of Yellow Fever in East Africa** (*vide* page 4).

Control measures come under three headings:—mosquito control, quarantine and inoculation. It is of paramount importance that *Aëdes aegypti* should be eliminated from seaports, ships and dhows on the sea or the great lakes, inland urban centres and aerodromes, railway premises, and all premises near stations and stopping places. The usual certificates are recommended; that declaring vaccination stipulates that it should have been done not less than 14 days and not more than two years before the traveller was last exposed to yellow fever infection.

It is desirable that all those who may be likely to travel by air in Africa, and that all troops in certain areas, should be vaccinated; mass vaccination of the entire indigenous population inhabiting a ten-mile strip along the coast of Kenya is desirable and justifiable, if it can be carried out. Viscerotomy services should be instituted, and more mouse protection tests carried out. *C. W.*

LE VAN (James H.). **Methods for controlling *Aëdes aegypti* Mosquitoes with *Gambusia holbrooki* Minnows at Key West, Florida.**—*Public Health Rep.* 1941. June 6. Vol. 56. No. 23. pp. 1217–1221. With 4 figs. on 2 plates.

At Key West, Florida, there is perennial infestation with *Aëdes aegypti*, which breeds principally in cisterns and wells; at the time of this study the city had no public water supply, and cisterns and other containers were in general use for collection and storage of rainwater. *Gambusia holbrooki* is found in fresh water ponds on Stock Island near Key West. The author stocked 2,754 cisterns, wells and receptacles with the minnows, after placing them overnight in water chorinated to 0·1 to 0·15 parts per million of residual chlorine to

prevent the introduction of bacterial contamination with the fish. It was found that Gambusia could not clean up water heavily infected with larvae, and in such cases the water was first covered with kerosene and the fish introduced when the larvae were killed. The film of kerosene did not seem to harm Gambusia.

After eight months 2,376 containers and wells were inspected; 1,105 contained fish, and in only eight of these were larvae found, whereas in 1,271 from which the fish had disappeared, larvae were present in 632. Many of the cisterns had in the meantime been pumped dry and refilled without restocking, and the fish had disappeared from many wells, probably having been removed by children. Educational measures have been undertaken and have met with some success, since requests for restocking with Gambusia have now been received. Detailed figures of the investigations are given. *C. W.*

Le Van (James H.). **Present-Day Methods for controlling** *Aëdes aegypti* **Mosquitoes.**—*Public Health Rep.* 1941. Sept. 19. Vol. 56. No. 38. pp. 1875–1880. With 4 figs. on 1 plate.

The information contained in this paper is much the same as that abstracted in this *Bulletin*, 1941, Vol. 38, p. 70. *C. W.*

Smith (Hugh H.), Calderón-Cuervo (Hector) & Leyva (José Pablo). **A Comparison of High and Low Subcultures of Yellow Fever Vaccine (17D) in Human Groups.**—*Amer. Jl. Trop. Med.* 1941. July. Vol. 21. No. 4. pp. 579–587.

A comparison of the results of vaccination in human groups with three lots of yellow fever vaccine, each prepared from the 17D strain of virus evolved from the Asibi strain [see this *Bulletin*, 1936, Vol. 33, p. 623]. One lot of vaccine was prepared from virus that had been maintained in tissue culture media for 342 passages, the second and third lots were prepared from seed virus of the 212th and 450th subcultures respectively. Each of the vaccines was prepared by inoculating the culture virus into 7-day-old developing fowl embryos and incubating for four days, then pooling the embryos and triturating in a ball-mill. A 10 per cent. suspension of this ground-up tissue is made in normal human serum, the mixture centrifuged for 30 minutes at 3,000 r.p.m., after which the supernatant fluid is filtered through a Seitz E.K. filter disc at 10 lb. pressure. The vaccine is distributed into ampoules, then frozen and dried in vacuo, after which it is submitted to the usual tests in both mice and rhesus monkeys.

The human groups used for this study comprised adult males between 20 and 50 years of age, who had been born and had lived continuously on the high savannah around Bogotá. Before vaccination the sera of all the men were tested for yellow fever antibodies. The men were then vaccinated with varying doses of active virus and their sera tested for the development of antibodies by protection tests in mice. No significant difference was found in the immunizing efficiency of the three lots of vaccine. With dosages approaching 100 m.l.d. for mice, some individuals failed to produce demonstrable antibodies, whilst other persons showed definite immunity after as little as 10 m.l.d. for mice, with both high and low sub-culture virus.

E. H.

SELLARDS (Andrew Watson). **Immunization against Yellow Fever with a Consideration of the Effects of a Virulent Neurotropic Strain on the Central Nervous System of Monkeys.**—*Amer. Jl. Trop. Med.* 1941. May. Vol. 21. No. 3. pp. 385–397. [25 refs.]

A general discussion of vaccination against yellow fever, in which the author emphasizes the opinion that effective immunization requires the injection of living modified virus and the development of an infection.

In view of the severe reactions which sometimes follow the use of living neurotropic virus from mice, the author made some experiments, using very dilute suspension of the French neurotropic strain injected intracerebrally into monkeys. The results are given in the accompanying table, from which it is seen that when the dilution reached 1 : 5,000,000 or 1 : 10,000,000 the inoculation of 0·1 cc. or less into the cisterna magna of monkeys produced no clinical symptoms but four out of five were immunized :—

TABLE I.

The effect of neurotropic yellow fever virus on the central nervous system of monkeys.

Number of Monkey	Injection of Rhesus Monkeys. Dilution of infective mouse brain ; 1 to	cc. of dilution	Route of Injection	Onset of fever	Result	Protective effective of serum for mice
				day		
Experiment 1						
1	100,000	0·05	Cisterna magna	6	Died‡	
2	1,000,000	0·05	Cisterna magna	8	Died‡	
3	1,000,000	0·1	Cisterna magna	8	Died‡	
4	10,000,000	0·1	Cisterna magna	11	Well	Complete
Experiment 2						
5	5,000,000	0·1	Cisterna magna	6	Well	Complete
6	10,000,000	0·03*	Cisterna magna	None	Well	None
7	10,000,000	0·05	Cisterna magna	8	Well	Complete
8	10,000,000	0·1	Cisterna magna	12	Well	Complete
9	10,000,000	0·05	Cerebrum	None	Well	None
10	10,000,000	0·1	Cerebrum	None	Well	None
Experiment 3						
11	1,000,000	0·1	Cerebrum	5	Died‡	
12	5,000,000	0·1	Cerebrum	9	Died‡	
13	10,000,000	0·03*	Cerebrum	None	Well	None
14	10,000,000	0·05	Cerebrum	5	Died‡	
15	10,000,000	0·1	Cerebrum	None (?)	Well	Complete
16	100,000	0·1	Subcutaneous†	9	Died‡	
17	100,000	0·1	Subcutaneous†	None	Well	Complete

*Estimated. † With gross trauma of frontal lobe. ‡Encephalitis.

The inoculation of similar doses intracerebrally was usually followed by death from encephalitis. Out of two monkeys with gross trauma of the frontal lobe, inoculated subcutaneously with larger doses, one died of yellow fever and the other remained well and developed immunity. It is stated that accidents of vaccination have occurred in any form of technique in which living virus is employed, and up to the present patients have shown symptoms of meningitis, encephalitis or myelitis, followed by complete recovery without sequelae.

The author states that sero-vaccination has limited possibilities, for on some occasions many of the patients failed to develop a protective serum and a few of these persons subsequently developed yellow fever, some of the infections being fatal.

He considers that there is opportunity for improvement in any of the techniques in use at present and that they do not represent, in detail, the methods which will eventually be developed for vaccination against yellow fever. *E. H.*

Findlay (G. M.). **Our Present Knowledge of Yellow Fever.**—*South African Med. Jl.* 1941. Apr. 26. Vol. 15. No. 8. pp. 143–144.

Portuondo Barcelo (J. M.). Fiebre amarilla. Tifus icteroides. Vómito negro. Algunas consideraciones sobre la etiología, epidemiología y sintomatología de esta enfermedad. Importancia del problema amarillo en el status sanitario de Cuba. [**Yellow Fever: General Considerations and Importance in Cuba.**]—*Rev. Méd.-Quirúrg. de Oriente.* Santiago de Cuba. 1941. Sept. Vol. 2. No. 3. pp. 172–181.

Bablet (J.). Sur l'organisation antiamarile au Brésil. [**Organization of the Yellow Fever Service in Brazil.**]—*Bull. Soc. Path. Exot.* 1940. Vol. 34. Nos. 1–3. pp. 5–15.

RABIES.

A Review of Recent Articles. XXXVI.*

i. *Virus.*

The work of Bernkopf and Kligler[1] on the cultivation of rabies virus in developing chick embryos has been summarized in this *Bulletin* on various occasions (1938, Vol. 35, p. 641; 1939, Vol. 36, pp. 193 and 724; 1941, Vol. 38, p. 494). The characteristics of the virus, which is now in its 47th passage, are further discussed. It shows no enhancement of virulence for the chick embryo as judged by the fact that the embryos develop normally, by the relatively low titre in the embryo brain (1 in 1,000 to 1 in 10,000) and by the scanty pathological changes in the brain. Virulence for mice and guineapigs remains unchanged, whilst that for rabbit is considerably reduced, as demonstrated by the prolonged incubation period (11 to 13 days) and by the duration of infection. The specific antigenic character of the chick embryo virus remained unchanged during 47 passages over a period of 18 months.

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*For the thirty-fifth of this series see this *Bulletin*, Vol. 38, p. 494.

[1] Bernkopf (H.) & Kligler (I. J.). Characteristics of a Fixed Rabies Virus Cultivated on Developing Chick Embryos.—*Proc. Soc. Experim. Biol. & Med.* 1940. Oct. Vol. 45. No. 1. pp. 332–335.

Dawson[2] has carried to a further stage his investigations on the propagation of rabies virus by inoculation directly into the chick embryo brain. It will be remembered that in his earlier experiments he found that subpassage by this method was simple and constant, and that the brains of chicks killed on the six or seventh day contained "an enormous number of Negri bodies" [this *Bulletin*, 1940, Vol. 37, p. 191]. He is now confirmed in his belief that "the chick embryo brain is an ideal medium for the propagation of rabies virus." He gives the histories of three strains which now have been carried through 65, 25 and 3 subpassages respectively. No gross pathological changes were observed until the third or fourth embryo-generation, when a mild hydrocephalus was noticed. In later generations this was more severe, being detectable as early as the third or fourth day, and thereafter increasing rapidly. The entire ventricular system was dilated, and the subarachnoid spaces enlarged, especially in the neighbourhood of the cerebellum. Symmetrical haemorrhagic necrosis of the tectum and forebrain supervened in later generations. Microscopic examination revealed severe hydromyelia, encephalomalacia and myelomalacia. Negri bodies were abundant in the neurones and were diverse in size. Larger bodies were vacuolated and contained basophilic inner bodies. They were found in the retina, in peripheral ganglia, in the central nervous system, in ependymal epithelium and, phagocytosed, in large mononuclear leucocytes. Inoculation by other routes caused similar appearances.

The effects are thus profound and, as the lesions are observed as early as the third day and death is usually as late as the eleventh day, it appears that the chick is able to withstand a massive inoculation over a long period. "This remarkable ability of the embryo to withstand infection much longer than other hosts makes it possible to study the more mature lesions of rabies."

It was also found that chick embryo-brain passage was associated with a marked reduction in pathogenicity for rabbit and mouse, so great that it was possible to produce a "self limited non-fatal disease in rabbits by intracerebral inoculation, and in mice by subcutaneous or intramuscular injection of embryo passage virus." Tests showed that recovery from the mild disease is followed by a solid immunity to intracerebral inoculation of rabbit-fixed virus and mouse-passage virus. At present the embryo passage virus is still highly virulent for dogs, but "it is hoped that prolonged passage will bring about alterations in virulence for dogs, comparable to those which have occurred for rabbits." "From a practical point of view, such a strain of virus would be an ideal vaccine, since it would be possible to immunize the animal with a single dose of virus which actually produced a mild infection. It would of course be essential that the mild disease produced in this fashion be non-transmissible in nature." The pathological changes described are well illustrated.

Although, on account of its high sensitivity, the rabbit is the animal of election for the study of the Aujeszky virus, the use of the guineapig presents certain advantages. It will be remembered [this *Bulletin*, 1933, Vol. 30, p. 578] that Shope found that after subpassage the virus was 10 times more prevalent in the brain of the rabbit than in that of the guineapig; and that the guineapig is about 100 times

[2] Dawson (James R.), Jr. A Study of Chick-Embryo-Adapted Rabies Virus.—*Amer. Jl. Path.* 1941. Mar. Vol. 17. No. 2. pp. 177–188. With 1 text fig. & 15 figs. on 4 plates.

more resistant to subcutaneous dosage than the rabbit. He also noted that subpassage through the guineapig caused an actual attenuation of the virus. CARNEIRO[3] finds that intramuscular injection into the guineapig is much more effective than subcutaneous injection, and that the results obtained have the advantage of greater constancy. The period of incubation is regular and short—between two and three days—local pruritus is a constant symptom, the minimum lethal dose is approximately 1 cc. of a 1 in 2,500 emulsion. For these reasons he recommends the use of the guineapig in the routine diagnosis of the disease.

ii. *Pathology.*

A series of experiments has been carried out by HABEL[4] with the object of "determining the tissue site of anti-rabies immunity by observing any difference in the progression of peripherally introduced virus in normal and in immunized mice and guineapigs, as well as by the titration of virus-neutralizing properties of immunized rabbits." Both live virus vaccine protecting against 10 M.L.D. of fixed virus introduced intracerebrally and phenol vaccine protecting against 1 M.L.D. were employed. The test dose was 0·2 cc. of a 1 in 5 dilution of first passage guineapig street virus brain, injected into the right gastrocnemius. After 24 and 48 hours, and 10 days, portions of right gastrocnemius, right sciatic, lumbar cord, brain and spleen were emulsified and inoculated into three young Swiss mice. "Taking two deaths after the tenth day out of three mice injected with each tissue, or at least one death in which Negri bodies were found, as the criterion for the presence of virus, it was found that by 24 hours, street virus was not demonstrable in the muscles of the controls but was present in the sciatic nerve and had also reached the lumbar cord. In the mice immunized with the phenol vaccine, S.V. was demonstrated only in spleen at the end of 24 hours, in all tissues except spleen in 48 hours, and in the sciatic nerve, spinal cord and brain in 10 days. In the mice immunized with live virus vaccine, S.V. was present in none of the tissues after 24 hours, in 48 hours only in the muscle, and in 10 days in none." In these mice experiments the phenol vaccine was a poor immunizing agent, and either the test mice were relatively insusceptible or the S.V. was not highly virulent.

A similar series was carried out on guineapigs, and in this case the phenol vaccine was of high immunizing potency and the S.V. was virulent. Further experiments were carried out to determine whether emulsions from the above tissues were able to neutralize fixed virus *in vitro*.

The general conclusions from these experiments on mice and guineapigs were that in the controls the S.V. remained viable and perhaps multiplied in the muscle at the site of inoculation for at least four days, in spite of the fact that in the tissue neutralization test the muscle of the control rabbit was able to neutralize 100 M.L.D. of virus. Spread of virus in untreated animals to the peripheral nerve,

[3] CARNEIRO (V.). A cobaia no estudo experimental da doença de Aujeszky.—*Arquivos do Inst. Biol.* Buenos Aires. 1940. Vol. 11. pp. 97–106. [12 refs.] English summary.

[4] HABEL (Karl). Tissue Factors in Antirabies Immunity of Experimental Animals.—*Public Health Rep.* 1941. Apr. 4. Vol. 56. No. 14. pp. 692–702. [30 refs.]

thence to the spinal cord, apparently occurred within 24 to 48 hours, whereas progression in the central nervous system to the brain was more delayed.

Animals vaccinated with live virus vaccine showed virus only at the site of inoculation for as long as four days, and never in the peripheral or central nervous system.

In mice receiving a vaccine of low potency the spread of peripherally introduced S.V. appeared to be increased.

Dodero[5] and his co-workers report observations on the effect of anti-rabic immunization by dried and glycerinated cords on certain blood characters. As is well known, these present no striking features.

In the human subject they observed inconstant augmentations of polynuclear and eosinophil leucocytes, but no significant change in the Arneth index ; no change in chlorides ; and nothing significant regarding blood sugar and polypeptides. In 10 per cent. of cases there was a slight albuminuria. Globular resistance was diminished in 49 per cent. of cases and increased in 7 per cent.

In the experimentally treated rabbit they noted increase in blood chlorides both in plasma and cells, but no variation in the erythroplasmatic ratio ; an inconstant glycaemia not accompanied by glycosuria ; no alteration in polypeptides ; and albuminuria in 90 per cent. of cases during the period of paralysis, which increased till death.

iii. *Methods of Treatment and Statistics.*

Webster and Casals[6] recapitulate in fuller detail the results of investigations carried out by the American school on irradiated tissue culture virus. These have been summarized in previous reviews [this *Bulletin*, 1941, Vol. 38, pp. 161 and 496]. They conclude that " from a practical point of view culture virus has not yet proved a satisfactory source of rabies vaccine, due chiefly to its low content of virus. . . . Altogether the results of the experiments to date suggest that basically the immunizing potency of a vaccine is dependent upon virus content, that is that the immunizing antigen is the virus particle. . . . The findings point to a relation between number of mouse lethal doses required to immunize and body weight."

In a previous paper [this *Bulletin*, 1939, Vol. 36, p. 728] Kligler and Bernkopf[7] noted that mice receiving one dose (0·5 cc.) of formolized tissue culture virus by the intraperitoneal route were immune to a subsequent infecting dose of mouse brain virus given intraperitoneally. A modification of this procedure has now been tested on

[5] Dodero (J.) & Hoang-Tich-Try. Formule leucocytaire et image d'Arneth dans le traitement antirabique pasteurien.—*Rev. Méd. Française d'Extrême-Orient.* 1940. June–July. No. 6. pp. 235–238. With 1 chart.

Auffret (Ch.) & Dodero (J.). Quelques modifications humorales chez les Annamites traités par la méthode Pasteurienne.—*Rev. Méd. Française d'Extrême-Orient.* 1940. June–July. No. 6. pp. 239–242.

Dodero (J.). La résistance globulaire chez le Tonkinois normal et chez le Tonkinois soumis au traitement antirabique pasteurien.—*Rev. Méd. Française d'Extrême-Orient.* 1940. Nov.–Dec. No. 9–10. pp. 574–578. With 4 charts.

Auffret (Ch.) & Dodero (J.). Quelques modifications humorales au cours de la rage expérimentale à virus fixe du lapin.—*Rev. Méd. Française d'Extrême-Orient.* 1940. June–July. No. 6. pp. 243–248.

[6] Webster (L. T.) & Casals (J.). The Quantity of Irradiated Non-Virulent Rabies Virus Required to Immunize Mice and Dogs.—*Jl. Experim. Med.* 1941. May 1. Vol. 73. No. 5. pp. 601–615.

[7] Kligler (I. J.) & Bernkopf (H.). Immunization of Dogs against Rabies with Culture Virus.—*Science.* 1941. Apr. 18. Vol. 93. No. 2416. p. 383.

dogs " with most promising results." Of 9 control dogs, 7 died after injection of live culture into the neck muscles. Of 13 dogs immunized by an intraperitoneal dose of 10 cc. formolized tissue culture, or of a formolized suspension of infected mouse brain, all remained " perfectly well." Neutralization tests demonstrated the presence of antibodies in the sera of the treated dogs. The sera of the immunized animals were able to neutralize 100 mouse cerebral lethal doses of the virus.

At the Peiping Union Medical College 383 cases of persons bitten by rabid animals came under observation during the period July 1923 to August 1940. Of these 201 were afforded antirabic treatment (by killed phenol vaccine, except during the period October 1937 to October 1938, when dried cords were employed). Nine of the 201 (six treated by killed phenol vaccine) developed rabies, in spite of the fact that " most of them had superficial wounds located on one of the extremities, and most of them started treatment within the first 4 days after the bite." The remaining 182 were persons who either refused treatment, or were bitten by dogs which were proved to be normal. Amongst these, 18 cases of rabies occurred, in five of which " there was no wound." These are high mortality rates : 4·5 for the treated and 9·9 for the untreated. Yü[8] considers the possibility that the strain of street virus of the neighbourhood is one of unduly high virulence. That it is not similar to Koritschoner's reinforced virus is shown by the fact that Negri bodies were always found in the brains of the vaccinated persons who died from rabies.

Of the 201 treated persons, five exhibited post-vaccinal reactions. One (of Landry type) died, one " probably died," the remaining three recovered.

[This experience at the Peiping Institute presents very exceptional features : (1) the high mortality amongst the untreated who were not severely bitten and five of whom had no bite at all. (2) The unusually high mortality amongst the treated whose bites were not unusually severe, and (3) the very high proportion of post-vaccinal sequelae. Experimental examination of the characteristics of the Peiping street virus, of the strain of fixed virus employed at the Institute, and information regarding the characters of the vaccine and the tests to which it was submitted are clearly desirable.]

At the Pinheiros Institute in São Paulo, Brazil, during the first six months of 1939, Vaz[9] reports that 648 persons were treated with Fermi's vaccine. In no case did the treatment fail, nor were any post-vaccinal sequelae observed. The statistics are classified according to the system introduced at the Paris Conference. Treatment is administered at 281 stations. Since the inception of Pasteurian treatment in 1930, only one case of neuroparalytic accident has been reported amongst 7,920 persons treated.

During the year 1939, antirabic treatment by the method of Semple was administered at Shillong[10] and its 68 outstations to 1,986 persons. Of these, 10 died of rabies (0·50 per cent.), one on the second and

[8] Yü (T. F.). Rabies.—*Chinese Med. Jl.* 1941. Apr. Vol. 59. No. 4. pp. 326–338. [19 refs.]

[9] Vaz (Eduardo). Serviço antirrábico descentralizado do Instituto Pinheiros. Estatística do 1° semestre de 1939.—*Anais Inst. Pinheiros.* São Paulo. 1939. July. Vol. 2. No. 4. pp. 73–79. English summary (8 lines.)

[10] Shillong : King Edward VII Memorial Pasteur Institute and Medical Research Institute Twenty-Third Annual Report for Year ending 31st December, 1939 [Anderson (L. A. P.), Director]. pp. 1–2. Anti-Rabic Section. pp. 9–26. Statistical Tables—Anti-rabic Treatment.

one on the third day of treatment. One case of paralytic accident of the fatal ascending myelitis type is reported. " With this case, the number of paralytic accidents occurring as the result of treatment over the past 5 years, has been 1 in 4,520 persons treated."

iv. *Paralytic Accidents.*

During the period 1934-38, Uzman, Aksel and Tuncman[11] have observed six cases of paralytic accident at the Institute at Istanbul. Of these five occurred after treatment by living vaccine (Hoegyes–Philipps modified) and one after treatment by the killed phenol vaccine of Semple. The total number treated was 9,356, so that the percentage incidence was 0·64. Only one case terminated fatally. The six cases are described in meticulous detail. In one there was no history of a bite, in two there had been exposure to cold and great fatigue. The causation of such accidents in general is discussed, and the authors conclude that they occur more frequently with living than with dead vaccines.

v. *Rabies in Animals.*

At the desire of the Health Section of the League of Nations Gautier[12] has made a comprehensive study of evidence of the efficacy of the preventive vaccination of dogs against rabies.

The problem was discussed at the International Rabies Conference in 1927, and the finding, whilst sympathetic, was non-committal. In 1928 and 1931 the Committee of the *Office international des epizooties* stated that conclusions could not be framed until further observations have been made. The evidence is twofold ; in the first place there are the experimental studies made in the laboratory, and in the second there is a heterogeneous mass of data relating to practical applications in different countries. As is so often the case the former has illogically lagged behind the latter. Practical application has consequently tended to become empirical, conclusions being based upon incomplete information, and taking the form of unconvincing and often biassed statements. " More precision is required and even, let us make bold to say, more frankness."

The paper commences with a concise bibliographical study of experimental work, which the author summarizes as follows. There is " an impression of uncertainty. The ground is not solid ; it slips away at each step. Since the experiments are neither coherent nor concordant, they should be taken up once more, if possible with quantitative techniques permitting of the comparison of results and

[11] Uzman (Mazhar-Osman), Aksel (Ihsan Schukru) & Tunçman (Zekai-Muammer). A propos des accidents paralytiques survenant au cours de la vaccination contre la rage.—*Arch. Balkaniques de Méd. Chirurg. et Leurs Spécialités.* Paris. 1940. Jan.–Mar. Vol. 2. No. 1. pp. 22–34. With 4 figs.

[12] Gautier (R.). The Preventive Vaccination of Dogs against Rabies. A Critical Review.—*Bull. Health Organisation.* (League of Nations.) 1940–41. Vol. 9. No. 3. pp. 269–326. [Numerous refs.]

based on the employment of better defined biological agents. A start has been made in this direction. . . . It seems to have been demonstrated that, under certain experimental conditions, the dog may be preventively vaccinated against rabies. But this is not enough. We want to know definitely whether or not it is possible to confer a sufficient degree of immunity on the dog by means of a single injection of vaccine, no matter of what kind provided its innocuity is certain!" The start to which Gautier refers is the mouse protection test introduced by WEBSTER and his co-workers at the Rockefeller Institute—a test whereby it is possible to assess the degree of immunity conferred precisely in terms of M.L.D. A further advance lies in the possible utilization of a culture virus of uniform and stable character. Much work remains to be done, but a start has been made.

When one turns to records of practical applications the state of affairs is still more unsatisfactory. The author using the machinery of the League of Nations received reports from institutes throughout the world. Some have achieved results which are apparently favourable, others have had no success. The stray-dog, jackal or wolf obtrudes itself. In countries where these are rife canine prophylaxis necessarily is of little value, whilst in converse circumstances some success may be achieved. The data even in the most advantageous circumstances are usually incomplete; the total canine population can seldom be even approximately estimated; the percentage of rabies cases amongst the non-vaccinated is not known. Where possible Gautier has had recourse, as an index of the efficiency of canine prophylaxis, to a reduction in the number of persons applying for Pasteurian treatment. The results are conflicting, and even though observed they might equally well be due to other coincident factors, such as the spontaneous decline of an epidemic, the enforcement of more drastic police measures, etc. Indeed, wherever public attention is focussed upon the ravages of a disease by the advocacy of some particular health measure, the mere fact that attention has been focussed leads to a tightening up of sanitary precautions in general, and often to a beneficial result which may have nothing to do with the health measure in question.

Reports from the various countries are dealt with in some 40 pages of the paper. With regard to these Gautier writes:—"Of the results referred to above, the most conclusive in our view are those relating to Hungary, where rabies, both in vaccinated and in non-vaccinated dogs has entirely disappeared from the regions in which compulsory immunization was enforced before 1938, and where a significant decline was observed in the number of persons having recourse to Pasteur treatment. It is worth recalling that, in Hungary, dogs receive one inoculation only. This is an instance of that flagrant contradiction between practical application and the experimental data, to which we have alluded at the beginning of the study. In this case, however, we do not hesitate to put our faith in the practical results."

[Even this result appears to the reviewer to be inconclusive. Sanitary measures were extraordinarily strict—dogs were under very complete control—the focussing of attention had been very great. Though canine rabies was stamped out, the figures show that the decline of canine rabies, and, in one district at least, of persons obliged to undergo treatment had set in prior to the introduction of compulsory canine vaccination, thus:—

Region	Date of introduction of compulsory vaccination	Number of cases of canine rabies				Number of persons treated		
		1933	1934	1937	1938	1933	1937	1938
City of Budapest...	Spring, 1935	70	27	2	0	1,529	423	413
Transdanubia ...	Autumn, 1936	505	248	13	2	1,714	306	195
County of Pest ...	Spring, 1937	231	152	65	0	1,996	620	407
Northern Counties	Spring, 1938	266	117	225	42	966	1,363	620
South-Eastern Counties	Spring, 1939	166	114	95	80	640	480	439

Moreover, in other countries similar measures were adopted without success.]

In summarizing the general results of his study Gautier remains non-committal. "At a time when supporters and opponents of preventive canine vaccination still confront one another any conclusion would be out of the question." He pleads for further experimental work, and for fuller statistical information regarding field tests. Finally he emphasizes the epidemiological importance of the stray dog [or jackal] which cannot be reached by any measure of prophylactic vaccination. The destruction of these rabies carriers will always be necessary for the safeguarding of the human community. "This implies that, amongst sanitary police measures, the preventive vaccination of dogs should be considered merely as an auxiliary."

The problem of the epizoology of rabies in South Africa is peculiar in that the dog plays a negligible rôle in the dissemination of the disease, the main carriers being wild carnivora of the mongoose family and in particular *Cynictis penicillata* (variously called the yellow mongoose, the yellow meercat, the red meercat).

An exhaustive study of the whole problem is presented by SNYMAN.[13] This covers a wide field of observation and experiment, which, on account of the peculiar nature of the South African problem is mainly of local interest and application. Readers of reviews of South African work during recent years are already aware of the main facts.

After a general historical and geographical survey SNYMAN describes in detail the areas affected, and the epizootics which have occurred. Then follow descriptions of the various meercats, their habitat, their food, and their distribution in relation to the areas affected.

The main thesis of the paper then follows: a comprehensive examination of methods of destruction of the animals which carry the disease. This involves a study of the structure of meercat burrows, and the nature of these is illustrated by interesting sketch plans. Gassing, trapping, explosion of burrows, baiting are in turn discussed. The description of gassing experiments involving the use of HCN, is reminiscent of the work of the Indian Plague Commission on the destruction of rats on shipboard and in granaries. Methods and apparatus are very similar. Determination of the minimal lethal concentration for meercat destruction under experimental conditions and in natural burrows; the effects of gassing along with the use of compressed air; the influences of dust and soil humidity, and of

[13] SNYMAN (P. S.). The Study and Control of the Vectors of Rabies in South Africa.—*Onderstepoort Jl. Vet. Sci. & Animal Industry*. 1940. July & Oct. Vol. 15. Nos. 1 & 2. pp. 9–140. With 9 graphs (1 folding), 10 illustrations, 5 sketches, 2 figs. & 6 maps. [106 refs.]

airlocks are dealt with in detail. Experiments with carbon monoxide, sulphurous gases, and heavy gases such as carbon bisulphide are also discussed.

Methods of trapping are described and illustrated. The results following the use of explosives were disappointing. Poisoning was abandoned on account of the risk to domestic animals. Thereafter follow descriptions of large scale field experiments carried out in various districts.

As the result of all these observations it was found that gassing of burrows with calcium cyanide dust followed by trapping was the most effective measure for the destruction of meercats. The method is "cheap, simple, and, with care, simple to handle, eliminating many elaborate precautions." In order to ensure success, attention must be paid to the following details: (1) All colonies must be located; (2) The veldt must be "systematically combed to ensure that all the meercats have been chased into the burrows prior to gassing"; (3) Fumigation must be thorough; (4) All disused holes must be closed; (5) Colonies must be systematically revisited and traps set where required; (6) Trapping must be continued as long as operations are being carried out.

The author concludes by stating that if the above procedure be followed, "it is a practical proposition to exterminate *Cynictis penicillata*, the principal carrier of rabies, together with *Suricata suricatta* and *Geosciurus capensis* in an area up to 10,000 morgen [*i.e.* about 20,000 acres] in extent, infected with rabies." He recommends a scheme for the "total eradication of rabies in the Union, by destroying the meercats in infected centres, first in the sparsely infected areas, and then by gradually closing in on the central infected areas."

vi. *Miscellaneous.*

As the result of crossed immunity tests on rabbits, and by the inoculation of virus-serum mixtures Dodero[14] in an extensive series of experiments has found no evidence of any immunological relationship between the viruses of rabies and of vaccinia. The sera of five patients suffering from variola did not neutralize rabies virus either *in vivo* or *in vitro*. *A. G. McKendrick.*

Gallo (P.) & Iturbe (J.). Primeros estudios sobre la rabia paralítica del ganado en Venezuela. [**Studies on Paralytic Rabies in Venezuela.**]—*Rev. Med. Vet. Parasit.* Caracas. 1939. Vol. 1. pp. 91–166. [Summary taken from *Vet. Bull.* 1941. Dec. Vol. 11. No. 12. pp. 860–861. Signed Miller Watson.]

The history of paralytic rabies in Venezuela and the symptoms of the disease are described. From experimental work the authors found that the virus is infective at a dilution of 1 : 5,000, passes through Berkefeld V and all Seitz filters and is preserved by freezing and drying, etc.

The disease was transmitted experimentally to cattle, horses, sheep, swine, dogs, cats, birds, and laboratory animals by intracranial, intraocular, and intravenous inoculation, but not by intraperitoneal

[14] Dodero (J.). Rapports immunologiques entre la rage, la vaccine et la variole. —*Rev. Méd. Française d'Extrême-Orient.* 1940. June–July. No. 6. pp. 249–252.

inoculation. Material from the cerebrum, medulla, salivary glands, lachrymal glands, and saliva was infective whether filtered or not. Bile, faeces, urine, abomasal contents, parenchymatous organs, and lymph nodes were not infective. Street virus injected intracranially set up infection after an incubation period of 17–29 days. Material from the cerebrums of unborn calves of infected mothers proved infective. Infection was not set up by feeding infective organ material or milk from infected animals. The virus became more virulent after passage.

The authors agree that the disease is transmitted by blood-lapping bats which can carry the virus in the blood without showing symptoms of disease. The bats infect each other by biting; they can live for several days without feeding and fly very fast for considerable distances. Non-blood-lapping bats, infected naturally or experimentally, may become carriers of the virus.

Cross-immunity tests indicate that the virus is identical with typical rabies virus. There does not appear to be any cross-immunity with the virus of equine encephalomyelitis of Venezuela.

The authors managed with difficulty to cultivate the virus on chick embryos, only one experiment in 24 being successful. Embryonic membranes are infective to laboratory animals after three days' incubation. After 7–9 days of growth specific bodies can be seen macroscopically on the membranes; they are between those of psittacosis and laryngotracheitis in size. There are also eosinophile granulations. The incubation period of the disease produced by chick-embryo virus is inconstant. Serial passage of virus in chick embryos becomes difficult, since many embryos do not become infected.

The authors were unable to obtain evidence that ticks are concerned in the transmission of the disease.

They vaccinated 4,000 cattle with phenolized vaccine (street virus), prepared from the cerebrums of naturally infected animals, using Puntoni's technique, but with a higher concentration of virus in order to reduce the number of inoculations from 15 to five. The results were hopeful, the immunity produced being proportional to the amount of material injected and never lasting less than eight months. Experiments were also made with phenolized vaccines from chick-embryo virus, but the results were not conclusive. 500 animals also were vaccinated with dried, live virus, suspended in normal saline immediately before use. One injection was given subcutaneously and produced considerable local reaction as well as slight general reaction. In a small amount of work done the method appeared harmless and the duration of immunity considerable.

Among the prophylactic measures suggested by the authors are :— education of the public regarding the danger of bats; study of the localities where bats are found; destruction of bats (blood-lapping and others), destruction of their nests together with other methods of reducing their numbers, destruction of animals affected with paralytic rabies; protection of animals against bats by providing shelters, illumination at night, and by the folding of animals as close as possible to the farmstead; preventive vaccination, and control of animal transport.

HELMINTHIASIS.

MUELLER (Justus F.) & COULSTON (Frederick). **Experimental Human Infection with the Sparganum Larva of** *Spirometra mansonoides* **(Mueller, 1935).**—*Amer. Jl. Trop. Med.* 1941. May. Vol. 21. No. 3. pp. 399–425. With 7 figs. [28 refs.]

Self inoculations were undertaken by each author and the results were watched for several months.

The possibilities that were envisaged before these infections were that more spargana might come into being, by asexual reproduction, than were injected, and that they might degenerate into *S. proliferum*, that they might migrate and be lost, and that with them a bacterial infection might be introduced.

The spargana were got from an experimentally infected rhesus monkey under aseptic conditions and were washed in 1 in 10,000 merthiolate solution. The tip of the head, not over 2 mm. long and representing the scolex, was cut off from three spargana, suspended in normal saline and injected through a coarse hypodermic syringe into the subcutaneous tissue over the left biceps, two into Mueller and one into Coulston. Removals of the parasites were undertaken as follows. From Coulston, after 68 days, was removed a larva 50 mm. long which then lay beneath the deep fascia of the axilla and 12 cm. from the site of injection ; from Mueller, after 69 days, a larva 60 mm. long which lay within the biceps, while at the same time 10 mm. of the tail end of the other larva was excised. From Mueller, 98 days from the date of infection, the rest of the third worm was removed, presumably from the biceps, and measured 60 mm. long. This last was given orally to a cat which had no ova in the faeces, and grew to an adult 50 inches long. Ova collected from the cat's faeces for culture developed normally, and when about to hatch the coracidia were placed with species of *Cyclops*. These became infected and were fed to two rhesus monkeys. Some 27 weeks later active spargana were recovered from one of these monkeys, so that the use of man as an intermediate host has no apparent effect in lessening the vitality of the species.

" Symptoms associated with infection were local induration at the site of the worm, periodic giant urticaria, edema, and erythema. These periodic symptoms appeared to coincide with movements of the worm which from time to time broke out of the surrounding reaction zone, presumably liberating into the circulation walled off toxins. These periodic local reactions were attended by chills and fever and feelings of profound depression and malaise.

" Eosinophilia appeared, rising to 10 per cent. in Mueller on the 32nd day, and to 9 per cent. in Coulston on the 23rd to the 27th day.

" A positive skin reaction was elicited to scratch tests or intradermal tests with antigens prepared from *Spirometra mansonoides* adult and sparganum, *T. crassicollis* adult and cysticercus, *T. pisiformis* adult and cysticercus, and *T. serrata*. Also with the substance of a plerocercoid found in Great Lakes ciscoes. Antigens for intradermal use were prepared by Dr. J. T. Culbertson of Columbia University. They were not lipid free.

" While the subjects were still infected skin testing did not elicit any immediate reaction, only delayed reaction after about 10 or 12 hours.

" After removal of the worms the subjects developed an immediate reaction to skin tests, while retaining the delayed reaction. The delayed reaction in the case of the scratch tests is recurrent several times at 10 to 12 hour intervals.

" In over 60 control skin tests on volunteers only one ' false positive ' was obtained, and that in the case of a student who gave a history suggesting that he may at one time have been infected with a sparganum.

" The two authors still show strongly positive reactions to skin tests at the present writing (January 8, 1941), almost 20 months after removal of the worms.

" Complement fixation tests were unsatisfactory on the two experimentally infected humans, possibly because of the employment of too weak an antigen, or more probably because the serum was kept for too long a time before performing the tests.

" Pathological changes were extensive and in the nature of chronic inflammatory reaction, with local necrotic areas surrounding the worm.

" In both subjects the spargana exhibited migration, in one case penetrating and forming a gallery in the biceps muscle, in the other passing to the region of the axilla. Encapsulation though extensive was not sufficient to wall off the sparganа.

" With the establishment of *Spirometra mansonoides* as a potential human parasite physicians throughout the geographic range of the worm should be informed of its nature and educated to watch out for it. The use of antigens of tapeworm substance for diagnosis is recommended.

" It further appears that this parasite may constitute another potential waterborn disease throughout its range in the eastern United States, and render swimming in certain natural bodies of water carrying the copepod intermediate host, or the use of shallow well or spring water, etc., dangerous.

" Such antigens as we used are not specific, since they retain the lipid fraction. *Spirometra* antigens elicited positive reactions in hydatid disease patients. It is probable that a more specific antigen can be prepared by preliminary removal of the lipids before extraction."

Clayton Lane.

ITAKURA (Jun). Ein Fall von Ligula mansoni beim Menschen. [**A Case of *Diphyllobothrium mansoni* in Man.**]—*Okayama-Igakkai-Zasshi* (*Mitt. d. Med. Gesellsch. z. Okayama*). 1941. Jan. Vol. 53. No. 1. [In Japanese pp. 125–130. With 1 fig. [31 refs.] German summary p. 131.]

Infection with *Sparganum mansoni* occurred lately in Okayama in a woman of 34. A tumour on the inner side of the upper part of the left thigh diagnosed as " Atherom " was removed and contained two of these larval worms, one measuring 17 by 1·5 mm. and the other 14 by 2 mm. *C. L.*

BRANDT (F. A.). **The Differential Staining of the Hooklets of Tapeworms.**—*South African Med. Jl.* 1941. July 26. Vol. 15. No. 14. pp. 277–278. With 3 figs.

Demonstration of Taenia hooklets depends ordinarily on their refractive index being different from that of the surrounding medium or tissue. Haematoxylin-eosin staining of sections of hydatid scolices, for example, shows up in minute detail the general structure, but the hooklets remain unstained. The author, however, has found that methyl violet or basic fuchsin when strongly heated will penetrate the hard covering of the hooklet and then is not removed by

the usual treatment by acid and alcohol. He recommends the following methods, one with fuchsin and methylene blue, the other with methyl violet and neutral red.

" *No.* 1 : *Fuchsin-Methylene Blue.*

" (*a*) Remove wax and hydrate section by passing through benzol, absolute alcohol, rectified spirit to water.

" (*b*) Treat with hot, concentrated alcoholic basic fuchsin (Verhoeff's) by burning the alcohol, but being careful that the stain does not dry on the slide.

" (*c*) Treat with 95 per cent. alcohol for 30 seconds.

" (*d*) Wash well in tap water.

" (*e*) Treat with 2 per cent. aqueous sulphuric acid, controlling the degree of decolorization by microscopic examination.

" (*f*) Wash very well in running tap water to remove all traces of sulphuric acid.

" (*g*) Counterstain with a 1 per cent. aqueous methylene blue solution for two to three minutes.

" (*h*) Dehydrate and mount in neutral Canada balsam."

" *No.* 2 : *Methyl Violet-Neutral Red.*

" (*a*) Remove wax and hydrate sections as in No. 1.

" (*b*) Stain for five minutes with a 1 per cent. aqueous solution of methyl violet, keeping the temperature of the stain just below boiling point.

" (*c*) Fix with Lugol's iodine solution for five minutes.

" (*d*) Decolorize with 95 per cent. alcohol, controlling the degree of differentiation by microscopic examination.

" (*e*) Counterstain with 0·5 per cent. neutral red for five minutes.

" (*f*) Dehydrate in absolute alcohol and mount in neutral balsam."

H. H. S.

Brailsford (James F.). *Cysticercus cellulosae*—**its Radiographic Detection in the Musculature and the Central Nervous System.**—*Brit. Jl. Radiology.* 1941. Mar. Vol. 14. No. 159. pp. 79–93. With 12 figs.

While doing special health investigation at Birmingham, Brailsford found all the tapeworms sent for examination to be *Taenia saginata*, yet during the same period there was no instance during which he found in cattle its larval stage *Cysticercus bovis* ; but every year there were discovered in the City abattoir a number of pigs carrying *Cysticercus cellulosae*, the larval form of *T. solium*. This discrepancy, it is suggested, may be explained by the observation that the infection in the pig is usually heavy and obtrusive so that the carcass is condemned, and if a lightly infected one slips through the general prejudice against eating underdone pork makes for destruction of the parasite. On the other hand the sparse infection of the ox makes easy the overlooking of the parasite, and the general liking for underdone beef enables cysticerci to reach alive a new host.

All the patients Brailsford has found harbouring *C. cellulosae* have been men who have served in the army abroad, mainly in India. An X-ray picture does not show up a cyst till calcification has set in, and this usually implies a blind period of five years ; it is suggested that the deposit of calcium first takes place in the cyst's contents ; the radiographic appearances vary with the distribution of calcium and the pressure of the surrounding tissues—the cyst being rounded in heart or brain, flattened between muscle fibres. As to the suggestion that living cysts do little harm and that steps should not be taken to kill them, it is pointed out that they inevitably die as the host ages,

so that some effort to kill them early is justifiable. Striking reproduced photographs accompany the paper including, under the heading diagnosis, those of *Trichinella spiralis* and Sarcosporidia. *C. L.*

Ewing (Cecil W.). **Cysticercosis Epilepsy.**—*Brit. Med. Jl.* 1941. Aug. 23. pp. 263–265. [10 refs.]

Out of a large number of necropsies on patients in mental hospitals extending over thirty odd years, this is the only instance of cysticercus epilepsy seen by Ewing.

In a man in whom necropsy demonstrated a diffuse cysticercosis of the brain the clinical picture had been epilepsy with dementia. It differed little from idiopathic epilepsy, but there was a more rapid development of dementia, ending in death. The man was 31, an ex-soldier, and had a negative Wassermann reaction ; on a moderate computation upwards of 100 cysts were scattered over the surface of the cerebrum, mostly in the area fed by the middle cerebral artery. They projected into the cerebral ventricles, were present in the basal ganglia, mid brain and right cerebellar hemisphere. There were four in the wall of the left ventricle of the heart, none in the liver. Examination of some muscles showed infection. In some cysts the scolex was obvious. There was no tapeworm in the gut. *C. L.*

Dickson (W. E. Carnegie) & Willis (J. D.). **Cysticercosis of the Brain with Epilepsy and Papilloedema.**—*Lancet.* 1941. Oct. 11. pp. 415–417. With 2 figs.

" A case of *Cysticercus cellulosae* infestation with focal epilepsy is described, in which there were the unusual features of grossly raised intracranial pressure and rapidly increasing papilloedema, with a normal ventriculogram."

" The prognosis, though serious, is not, as has commonly been thought, uniformly bad."

Tornack (Joachim Hans). Ueber Zystizerkeninfektion. [**Cysticercus Infection.**]—*Deut. Med. Woch.* 1941. June 6. Vol. 67. No. 23. pp. 628–630. With 3 figs. [17 refs.]

A man of 44 was admitted to hospital for infarction of the lung. When examined by X-rays, heavy cysticercus infection of the thoracic muscles was disclosed, it being, as the figures show, equally extensive in the muscles round the pelvis and left lower limb.

He had indeed thrombo-phlebitis of the left leg. As to his cysticercus infection his battery in 1915 fed in Belgium on raw pork, and though two of his mates got tapeworms he noticed none in himself. He carried a linear scar 8 cm. long on the left side of the back of his head, caused by a hand grenade splinter in the battle of the Marne. He had a lump, described as a cysticercus, in the neck muscles, and suffered from convulsions. Blood was sent to the Hamburg Institute of Hygiene, which reported complement fixation in a titre of 1 in 20, but as the author had no antigen himself, the skin reaction was not attempted. Hydatid antigen gave negative results to both tests. Eosinophilia reached 4 per cent. References are limited to Axis publications from 1887 onwards. *C. L.*

Stunkard (Horace W.). **Tapeworm Infection in the West Indies.**—*Rev. Med. Trop. y Parasit.* Habana. 1940. Sept.–Dec. Vol. 6. Nos. 5 & 6. pp. 283–288. With 1 plate. [17 refs.]

Deschiens (R.) & Renaudet (R.). La réaction de fixation du complément dans le téniasis à *Taenia saginata.* [**The Complement Fixation Reaction in** *T. saginata* **Infection.**]—*Bull. Soc. Path. Exot.* 1940. Vol. 34. Nos. 1–3. pp. 17–25.

Hearin (James Thomas). **Studies on the Acquired Immunity to the Dwarf Tapeworm,** *Hymenolepis nana* **var.** *fraterna,* **in the Mouse Host.**—*Amer. Jl. Hyg.* 1941. May. Vol. 33. No. 3. Sect. D. pp. 71–87. [33 refs.]

"1. A high degree of acquired resistance is produced by an initial infection with *H. nana* var. *fraterna* against a second infection. This immunity was demonstrated in one series of experiments to be absolute for at least 102 days after the first infection. Data gained from subsequent experiments have shown that this immunity may remain absolute for 163 days.

"2. This absolute immunity to a second infection has been shown to become established in a series of mice as early as 12 hours after infection.

"3. It was demonstrated that the immunity remains absolute for at least 141 days after the removal of the initial parasite burden by repeated doses of tetrachlorethylene.

"4. No demonstrable active immunity was produced by experimentally introducing, by operation, the adult stage of this parasite in mice which harbored as many as twelve tapeworms for a period of 9 days before the second infection was administered.

"5. No active artificial immunity could be produced by the intraperitoneal injection of as much as 32 cm. of viable adult tapeworms as long as 14 days before infection.

"6. An almost complete immunity was produced in previously uninfected mice by repeated intraperitoneal injections of serum from immune animals. It was found that the greatest protection was conferred when all injections were given previous to test infection. These experiments, therefore, have demonstrated that the immunity to this parasite results from the development of humoral antibodies."

Senekji (H. A.). **Polysaccharide Scolex Antigen for the Immunological Diagnosis of Hydatid Disease.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1941. Mar. 27. Vol. 34. No. 5. pp. 401–403.

"The scolices are collected under aseptic conditions from the fresh fertile cysts from the liver and lung of sheep and cattle. They are then separated from the debris by centrifuging at a low speed, washed three times in saline, and finally resuspended in saline to which formalin is added in 0·1 per cent. concentration, and stored in the ice chest.

"The scolices of the different lots are pooled together and extracted in four volumes of pure acetone at 37°C. overnight. The sediment is collected by centrifuging, dried at 37° in the incubator, ground up in a clean mortar, weighed and stored in a $CaCl_2$ desiccator in the dark.

"Three grammes of the powdered scolex material are then extracted in 750 c.c. of N/4 trichloracetic acid for 48 hours in the ice chest. The supernatant, which is very opalescent, is separated by centrifuging.

On neutralizing the supernatant with 40 per cent. NaOH, a cloudy cotton-wool precipitate is immediately formed; the flask is then returned to the ice chest and kept overnight. The precipitate is collected by centrifuging, washed twice in absolute alcohol, once in ether, dried at 37°C. in the incubator, ground up into a fine powder in a mortar, weighed and stored in a desiccator in the dark. The yield is about 5 per cent. of the dried scolex. This powder retains its antigenic potency for a long time in the dark in the desiccator."

"Since the human hydatid fluid had been shown to have poor antigenic properties, it cannot be used for the laboratory diagnosis of hydatid disease. Sheep or cattle hydatid fluid is antigenically very potent. There may be considerable variation between the potency of one batch and that of another. The scolex antigen can be prepared in large amounts, and its keeping potency is good, especially in the powder form. It is a polysaccharide and is free of proteins. It is not only a haptene but is also a functional antigen. In the routine clinical laboratory diagnosis of hydatid disease by the specific allergy test of Casoni, it gives uniform and reliable results, because a constant uniform quantity of the antigen is used throughout the tests."

GREVAL (S. D. S.), CHANDRA (S. N.) & DAS (B. C.). **Complement-Fixation in Hydatid Disease: Suggestions.**—*Indian Jl. Med. Res.* 1941. Jan. Vol. 29. No. 1. pp. 203–207. [10 refs.]

"From carcasses of freshly slaughtered sheep fluids from a dozen or so cysts are collected by aspiration in separate bottles. To each bottle is added on the spot 0·5 per cent. of a mixture of equal parts of ether and trikresol. The bottles are shaken vigorously, brought to the laboratory and left in a refrigerator overnight. Next day the fluids are tested for anticomplementary and haemolytic activity. . . . In Calcutta a dozen fluids can be obtained sometimes on one day from the municipal slaughter-house."

"1. At least six phenolized, selected and pooled hydatid fluids from cysts of freshly slaughtered sheep yield a reliable and stable antigen for a complement-fixation test. It is kept in a refrigerator.

"2. The test is linked to the Wassermann reaction.

"3. A group reaction with sera from cases of hydatid cysts of *Cysticercus cellulosae* is possible. The fluid from the corresponding cysts in pigs is not readily procurable.

"4. The complement-fixation test as described can give measurable and repeatable readings which should indicate retrogression of the hydatid disease as a result of non-surgical treatment."

GREVAL (S. D. S.), CHANDRA (S. N.) & DAS (B. C.). **A Note on Complement Fixation in Hydatid Disease and Associated Considerations.**—*Indian Med. Gaz.* 1941. July. Vol. 76. No. 7. pp. 412–413. [12 refs.]

The antigen is hydatid fluid from freshly slaughtered sheep, selected, pooled, phenolized and preserved in a refrigerator. As a routine the suspected serum is used in dilutions of 1 in 10, 1 in 50, 1 in 100, and 1 in 200, the complement is in a dose of 2 M.H.D. During the last 11 months the tests in five cases have been held to be satisfactory. In one (dilution 1 in 100) the diagnosis was confirmed surgically and microscopically after a positive reaction, the same held in a second in

a dilution of 1 in 50, and in a third in that of 1 in 25 ; a patient with fits and cysts showed a positive reaction in dilution 1 in 40 ; a fifth with a reaction at 1 in 10 was left as a doubtful diagnosis. In India since 1933 the hydatid infections reported have numbered 46. *C. L.*

CULBERTSON (James T.) & ROSE (Harry M.). **Further Observations on Skin Reactions to Antigens from Heterologous Cestodes in Echinococcus Disease.**—*Jl. Clin. Investigation.* 1941. May. Vol. 20. No. 3. pp. 249–254. With 2 figs. [19 refs.]

" Antigens suitable for eliciting skin reactions in patients with echinococcus disease can be derived from many different cestodes, including (in addition to the specific larval parasite *Echinococcus granulosus*) *Taenia serrata, T. saginata, T. crassicollis, Hymenolepis fraterna, Moniezia expansa, Raillietina cesticillus* and both the adult and sparganum of *Diphyllobothrium mansonoides.*

" These antigens will also elicit skin reactions in normal persons locally sensitized passively with the serum from patients with echinococcus disease." *C. L.*

BARNETT (Louis). **Multiple Abdominal and Pelvic Hydatid Cysts (Peritoneal Cysts) ; a Study of 228 Cases.**—*Australian & New Z aland Jl. Surgery.* 1941. Jan. Vol. 10. No. 3. pp. 223–233. With 7 figs.

Of the 1,450 records, filed in the Hydatid Registry of the Royal Australasian College of Surgeons up to the end of 1939, about 16 per cent. may fairly be classed as peritoneal.

The preponderance of males so infected over females is not held to be due to predisposition, but to the greater likelihood of a hydatid cyst in a man being ruptured by violence (for this is what is believed to happen in 99 per cent. of cases) a leakage in youth being perhaps insidious and overlooked or even forgotten. It is noteworthy that DÉVÉ holds that 22 per cent. of hydatid cysts rupture sooner or later and that a fertile cyst of average size contains about two million scolices. A rupture into the peritoneal cavity allows these to scatter over it, they may be found dispersed in myriads decently interred in a fibrocellular shroud, one autopsy having revealed 1,089 in a person 45 years old. Obviously most scolices die, but it must be gravity that takes them into the pelvis in upright man, for when scolices are deliberately injected into the peritoneum of a quadruped they remain about the omentum and mesentery. Equally, when scolices get scattered on the wound in the abdominal wall, through which the peritoneum is reached, they may grow in it.

In only 16 persons was there a clear history of previous injury (such as might have ruptured a parent cyst) followed by acute abdominal symptoms and anaphylaxis. The late symptoms are those of pressure and the tense cysts may rupture into viscera, sometimes widely, as in the man of 35 who coughed up and vomited cysts and passed others in urine and faeces.

Prognosis is not so bad as painted, for the Registry has records of patients coming under surgeons' hands 20 times or more and coming up smiling for yet one more operation ; one indeed survived 28 but died under the 29th. Most live for years and may even reach old

age. Deaths have been 16 per cent., but many patients are still infected and may die later. When an operation becomes necessary too much should not be done at one sitting; pedunculated or near pedunculated cysts may be completely excised, sessile ones may be emptied after preliminary cautious formolage, but the adventitia should be left and the opening of the emptied cavity oversewn. At the first operation aim at manual abdominal exploration to discover the original cyst, but be gentle and beware of bursting a thin-walled cyst, and if there should be recent rupture swab abdominal reces es with ether as Dévé advised; formalin is too irritant. Septic cysts of course need drainage, others do not. Pelvic cysts are apt to be a surprise to the gynaecologist; in three of the 228 patients these cysts have made Caesarean section necessary, they should be operated on by the abdominal route without undue delay. *C. L.*

Calvo Melendro (J.). Equinococosis peritoneal múltiple. [**Multiple Peritoneal Hydatids.**]—*Rev. Clin. Española.* 1941. Apr. 1. Vol. 2. No. 4. pp. 359–363. With 1 fig.

These are reports on two patients with multiple hydatid cysts of the peritoneal cavity, both from the Soria Province of Spain.

In one the primary nature of the infection is held to be established, since neither at operation nor autopsy on this girl of 11 was there discovered the remains of a ruptured parent cyst that had burst and seeded the abdomen. At operation one cyst was shelled out of the liver and 24 were removed from the peritoneum, while autopsy revealed three more in the liver. The other patient, an unmarried woman of 27, recovered from operation during which there were found signs of previous inflammation, cysts of the peritoneum ranging in size from a nut to an orange, and one attached to the lower face of the liver from which it was easily stripped. Only those cysts from over the iliac fossae were multivesicular. *C. L.*

Jacobo Spangenberg (Juan), Belgrano (Carlos Rossi) & Zunino (Emilio). Ascitis biliar. Coleperitoneo hidatídico. [**Biliary Ascites of Hydatid Origin.**]—*Semana Méd.* 1941. Aug. 14. Vol. 48. No. 33. pp. 391–398. With 6 figs.

A man of 49 died two years after acute abdominal symptoms (pain and vomiting) had come on; he had been aspirated to the extent of 7 and 10 litres, but the ascitic fluid did not suggest on examination that it had come from a ruptured hydatid cyst. Necropsy showed a thick walled hydatid cyst in the left lobe of the liver, as big as an orange and communicating both with the peritoneum and the bile passages. The peritoneum contained bile-stained fluid with some small unfertile hydatid cysts and the cavity in the liver contained some remnants of the hydatid membrane. *C. L.*

García (Juan C.). La uncinariasis en la provincia de Corrientes. [**Hookworm Infection in the Province of Corrientes.**]—*Bol. Sanitario.* Buenos Aires. 1940. Sept.–Dec. Vol. 4. Nos. 9, 10, 11 & 12. pp. 615–627.

Combating of hookworm infection on a mass scale may either be by the institution of dispensaries to which the people come, or by a sanitary campaign in which the staff go to the people.

The setting up of a dispensary in a centre of population excites interest and induces cooperation ; later both decline, but the dispensary may continue to play an important part in the sanitary campaign. This last may take one of three lines : (*a*) The intensive method with a census of the population, examinations of the faeces of all persons, treatment of all infected and the construction of latrines. Its inconveniences are held to be : (1) all stools will not be got ; (2) light infections will probably escape detection ; (3) many will refuse treatment ; (4) only in small communities can it be put through. (*b*) Mass treatment in the sense that if preliminary test examinations show 50 per cent. infected the whole population will then be treated. (*c*) Smillie's method, namely treatment of the sick. In this method, since it is held that larvae do not live in the soil for more than two months and infections are got little by little, varying procedures are employed : (1) with heavy infections and no latrines (no evidence of cooperation) there is a yearly treatment to reduce infection to a carrier state ; (2) where the building of latrines is possible three treatments are given, thus getting time to erect latrines in three-fourths of the houses, and thereafter another campaign of treatment and of propaganda intense enough to persuade the people to have latrines in all houses ; (3) with light infections, treatment and latrine erection. There is sketched the way in which, since SMILLIE worked in 1922, the campaign has developed in the Province, and particular mention is made of the activities of the Penna Institute, which have resulted in the lessening of numbers of the sick and in increasing capacity for work. An issue of a six-monthly certificate of deparasitization to a population in which 39 per cent. are illiterate is advised [presumably after re-examination and, if necessary, treatment].

C. L.

ÔHAMA (Sinken). **Observations on Hookworm Disease in Isigaki Island, Okinawa Prefecture. II. Studies on the Mode of Infection of Hookworm among the Population in Kabira Village, especially on the Relation of Soil Infection by Hookworm Larvae to Occupation and Habits of the Population, Domestic Animals, Soil and Atmospheric Phenomena.**—*Taiwan Igakkai Zassi* (*Jl. Med. Assoc. Formosa*). 1941. July. Vol. 40. No. 7. [In Japanese pp. 1212–1223. With 1 map. English summary p. 1223.]

In Isigaki island the maximum temperature is 26·41°C., lowest 20·25°, average 23·31° ; rainfall is 2,296 mm., average humidity 78·8. The highest rate of infection with hookworm larvae in soils was 100 per cent. in melon fields, 27·3 in sweet potato fields, 25 in mulberry fields and in vegetable manure heaps, 21·4 in sugar-cane fields. Sandy soil has more larvae than sandy humus ; clay contains fewest larvae.

In the faeces of 50 pigs Ascaris eggs were found in 21, *Strongyloides stercoralis* larvae in 1, and doubtful hookworm eggs in 2. *C. W.*

BUCKLEY (J. J. C.). **Observations on the Vertical Migrations of Infective Larvae of Certain Bursate Nematodes.**—*Jl. Helminthology.* 1940. Dec. Vol. 18. No. 4. pp. 173–182. With 12 diagrams.

The technique consists in making on a 3 × 1 in. glass slide by a writing diamond the marks seen in the figure. By brush or pipette infective nematode larvae are spread on the 2 mm. wide strip, some water is

added and allowed to evaporate almost to dryness. Fine sand that has passed a sieve with 100 meshes to the inch is sprinkled evenly on the slide, already moistened by breathing on it, and permanent adhesion of the sand is insured by spraying it with an atomizer ; the layer of sand must not be more than one grain thick. A mounted needle clears it from all parts outside the dotted lines, and these parts are smeared with a thin layer of vaseline, so preventing the larvae from straying off the observation surface.

Marked slide showing spacing of lines, in millimetres. The dotted line represents the vaseline border.

[Reproduced from the *Journal of Helminthology*, from block lent by the courtesy of the Director of the Institute of Agricultural Parasitology.]

The sand is a good medium for larval migration and also keeps moisture uniform ; to prevent loss of this last the slide has its 5·5 mm. attachment end set in a cut across a cork that fits into and is placed in a 4 in. by 1¼ in. glass tube. The mounted slides are so set that their surfaces were vertical, the unattached end being uppermost ; or the whole surface is horizontal when the effects of light are being investigated. In the latter case if it was a question of phototropism, one end is set towards a window and a piece of black paper is arranged 5 mm. above the other half. For testing migration in the dark the whole slide is so covered.

So far as the skin penetrating larvae of *Ancylostoma caninum* are concerned the vertical migration varied in direction with the temperature. Whether in the light or dark, migration was mainly downwards at temperatures between 11° and 14°C., mainly upwards between temperatures of 21° to 22°C. *C. L.*

Palmer (Eddy D.). **The Course of the Daily Egg Output during an Early Infection with the Hookworm** *Necator americanus.—Amer. J. Hyg.* 1941. July. Vol. 34. No. 1. Sect. D. pp. 1–12. With 1 fig. [27 refs.]

Palmer placed 50 infective hookworm larvae, after washing them, on the back of his hand. Counts were made by D.C.F.F. using as the floating fluid zinc sulphate solution of s.g. 1180.

" An experimental infection with *Necator americanus* was contracted by the writer in order to study the possibility of egg-production cycles occurring in early infections. Daily counts by the zinc sulphate centrifugal floatation technic were made from the beginning of the patent period on the 51st day of infection through the 151st day. It was found that during this period the 2-weeks cycle in egg output was correlated with a 2-weeks fecal-output cycle. Thus only a pseudo-cycle in egg production was found.

" Hookworm eggs were found to be unequally distributed through formed stools, so that an egg count of a random sample of formed stool did not provide a reliable estimate of the total egg contents of the stool. A reliable estimate was obtained, however, by sampling a homogeneous

water suspension of the whole stool. Egg counts expressed as eggs per milliliter of feces were found to be more reliable as indicators of a hookworm burden than counts expressed as total numbers of eggs passed per day, because the daily total egg outputs varied more than the egg contents per milliliter of feces.

"A comparison was made of the zinc sulphate centrifugal floatation technic and the Stoll egg-counting technic. Three modified Stoll dilution counts were made daily on the fecal suspensions for 67 days. While it was found that the dilution counts demonstrated more eggs than the zinc sulphate counts, it is shown that this difference was due to the fact that the zinc sulphate solution failed to float degenerate (unfertilized ?) eggs."

C. L.

Brown (H. W.) & Otto (G. F.). **The Differential Leukocyte Count associated with Hookworm Infection.**—*Amer. Jl. Dis. Children.* 1941. Apr. Vol. 61. No. 4. pp. 727–733. [11 refs.]

"It appears likely that eosinophilia occurs at some stage of infection with N. americanus, as has been suggested by Ashford and Igaravidez. On the other hand, eosinophilia is not always present in such infections, and in regions where the infection is common a high percentage of eosinophils may be present in patients whose feces contain no hookworm eggs. Our data may be explained by Ashford's suggestion that eosinophilia is associated with acute or recent infections, although they can hardly be said to verify his suggestion."

"The average percentage of polymorphonuclear eosinophils for the 53 children infected with hookworm was 11·7, whereas for the 68 worm-free children the percentage of eosinophils was only 6·6. Furthermore, the 29 more heavily infected children had, on the average, a higher percentage of eosinphils (13·0) than the 18 lightly infected children (9·3). However, none of them could be said to be very heavily infected and none of them had marked anemia, so that the higher percentage of eosinophils in the more heavily infected patients cannot be interpreted as being contrary to the suggestion of Ashford and Igaravidez that the eosinophilia disappears or is decreased in cases of long-standing, debilitating hookworm disease."

Pieraerts (G.). Etude sur le syndrome dépigmentationoedème au Kasai. (Première partie.) [**A Syndrome of Depigmentation and Oedema in Kasai.**]—*Bull. Soc. Path. Exot.* 1940. Vol. 34. Nos. 1–3. pp. 84–95.

One of the local names given to this syndrome is Diboba ; it occurs in persons with hookworm infection, and its clinical aspect, it is held, is dominated by the deficiency in iron which this infection causes, and by seasonal changes in food.

Stress is laid on change in the pigmentation of skin and hair. The black skin takes a chestnut, then an ochre, and lastly a yellow colour ; the lightening of the hair may continue till its colour may be that of rye straw. Moreover, in one whose illness has come on quickly the distal part of the hairs may be black and the parts near the roots light. Conversely, with cure, the hair becomes black first near its root while still light further from it, the changes are particularly obvious through a lens. [Such changes do not seem to have been reported in pure hookworm disease, but the others next cited are common when it is severe.] There are anaemia, murmurs over the heart and jugular

veins, oedema, ulcers and digestive troubles, diarrhoea being apt to end life. Puncture of lymph nodes disclosed no trypanosomes, the urine is normal and there are no other constant symptoms. The average percentage of haemoglobin in the blood varied in different groups between 62·4 and 42·4, the colour being least in those in whom oedema or pigmentation were greatest. The red corpuscles were ortho- or hypochromic and had little evidence of regeneration, there being few nucleated cells, which were normoblasts, and reticulocytes being fewer than normal. From September to December diet consisted mostly of unvaried manioc bread, and it was then that diboba was at its height. Three groups were treated, one of 18 with unworming and perchloride of iron showed remarkable progress, a second of 15 without unworming but with iron showed slight improvement, a third of 6 with unworming and no iron showed no improvement except a slight gain in haemoglobin. *C. L.*

Napier (L. Everard), Das Gupta (C. R.) & Majumdar (D. N.). **The Treatment of Hookworm Anaemia.**—*Indian Med. Gaz.* 1941. Jan. Vol. 76. No. 1. pp. 1–11. With 13 graphs.

The paper deals with investigations on 36 Indians (32 men, 3 women and 1 child) who showed hypochromic anaemia, and in whom hookworm infection seemed to be its sole cause.

In the absence of deficiency of dietary iron, absolute or relative, even a heavy load of hookworms produces no anaemia. Rice, particularly when polished, is poor in iron ; people whose food it is have little iron stored, are on the verge of iron starvation, and cannot meet in full the demands of blood loss or of pregnancy ; nor, to meet a coming demand, can the store be increased beyond the normal level. On the other hand, when diet is rich in iron the balance between absorption and loss of the metal can be maintained, in spite of a heavy hookworm load.

Of the 36 patients, 9 had less than 2,000 eggs per gramme of faeces, 10 had between 2,000 and 10,000, 17 had over 10,000 ; of 28 patients, 6 had achlorhydria, 6 had hyperchlorhydria and in 16 the acid was within the normal range. The egg count was below 2,000 per gramme in 5 of the 6 persons with achlorhydria ; of nucleated red cells got on sternal puncture between 30 and 50 per cent. were normoblasts in 20 of the 30 patients in whom this point was investigated. Reticulocyte response did not give a reliable prognosis. These are the conclusions drawn from observation of these 36 anaemic patients.

" Anthelmintic treatment without iron treatment is of little immediate value.

" Even in a very anaemic patient, a return to the normal haemoglobin level can be achieved by treatment with iron alone in most cases, but this level will not be maintained unless the hookworms are now removed.

" A slightly better response to iron treatment will be obtained after deworming, but the difference does not justify the risk of treating a patient with a very low haemoglobin level by anthelmintics.

" There was no evidence in the subjects under investigation of a copper or manganese deficiency, and there does not appear to be any advantage in adding these metals to the medicinal iron.

" There is some evidence that, grain for grain of metallic iron, ferrous ammonium sulphate in dextrose solution is a more efficient preparation than ferrous sulphate in tablet form.

" Two courses of treatment are usually both necessary and sufficient to raise the level of a very anaemic patient to the normal level ; the courses

we gave consisted of 18 grains of ferrous sulphate (exsic.), or 18 grains* of crystalline ferrous ammonium sulphate in dextrose solution, daily in two or three doses, for 3 weeks. It is suggested that 4 c.cm. of tetrachlorethylene as an anthelminthic be given in the interval between the two courses of iron administration. In mild cases, where only one course is likely to be necessary, the anthelminthic treatment can be given coincidently with the iron treatment.

"Our observations support the accepted theory that the anaemia of hookworm infection is due mainly to blood loss, but indicate that there is some other minor factor operating which we suggest is most probably failure of absorption as a result of intestinal mucosal dysfunction."

C. L.

Bodon (George R.). **A Case of *Strongyloides stercoralis* Infestation.**—*Jl. Lab. & Clin. Med.* 1941. July. Vol. 26. No. 10. pp. 1608–1611. With 5 figs.

"A case of an Italian immigrant woman is presented in which the stool examinations revealed rhabditoid larvae of *Strongyloides stercoralis*.

"It may be assumed that the parasite caused uncertain abdominal symptoms for which the gall bladder and the appendix were removed. Later two laparotomies were performed for the persistence of symptoms, which were thought to be due to postoperative adhesions. All operations resulted in negative findings."

"The stools of the husband and the children were also examined, and the parasite was found to be present in the husband's stool. The blood count of the husband showed eosinophilia of 10 per cent., but otherwise he did not show any symptoms which could be related to the presence of the parasite. Both individuals undoubtedly acquired the parasite in Italy."

Tomita (Susumu). **On Local Reaction of Infected Skin, Clinical Symptoms and Changes in Blood Picture in Experimental Human Infection with *Strongyloides papillosus* and *S. fülleborni*.**—*Taiwan Igakkai Zassi* (*Jl. Med. Assoc. Formosa*). 1941. Mar. Vol. 40. No. 3. [In Japanese pp. 427–442. With 7 charts & 6 figs. on 1 plate. [10 refs.] English summary pp. 442–443.]

The author describes the local pain and itching, and the local skin lesions produced, when infective larvae of *Strongyloides papillosus* and *S. fülleborni* are applied to the human skin. *S. papillosus* does not infect man, so that although there is penetration of the skin there are no general symptoms, but *S. fülleborni* does infect man, eggs are subsequently passed in the faeces and there may be general urticaria with or without fever. Eggs are found sometimes as early as 16 days after infection, and larvae have been found by faecal culture as long as 11 months after infection. The blood changes, which are slight, are referred to. [See this *Bulletin*, 1941, Vol. 38, p. 517.] *C. W.*

Estrada (Januario) & Garcia (Enrique). ***Ascaris lumbricoides* in the Common Bile-Duct : Report of a Case.**—*Jl. Philippine Med. Assoc.* 1941. July. Vol. 21. No. 7. pp. 331–336. With 1 plate. [30 refs.]

Ascaris has been found in the biliary passages after death. Its discovery there during life at operation is here described in two patients,

* "We are now using 44·5 gr. daily as originally prescribed, and getting even better results."

and in both of whom there were stones in the gall bladder. [Does not this suggest that the passage of a stone may so dilate the common bile duct that it no longer properly contracts and guards against intrusion of a worm ?] *C. L.*

Deschiens (R.) & Nicol (L.). Recherche et dosage des anticorps dans l'ascaridiose par la méthode de la fixation du complément. [**Antibodies in Ascaris Infection.**]—*C. R. Soc. Biol.* 1941. Apr. Vol. 135. No. 7–8. pp. 516–520.

Swartzwelder (John Clyde). *Toxocara cati* (**Cat Ascarid**) **Infection in Man. Report of an Additional Case.**—*Jl. Trop. Med. & Hyg.* 1941. May 15. Vol. 44. No. 10. pp. 61–62. With 1 fig.

"*Toxocara cati* infection in the human host is very infrequent, although the exact number of cases on record is not entirely clear. An additional, apparently authentic, case is put on record herewith."

DERMATOLOGY AND FUNGOUS DISEASES.

Du Bois. Le traitement des epidermophyties interdigitales. [**The Treatment of Interdigital Ringworm.**]—*Schweiz. Med. Woch.* 1940. Dec. 14. Vol. 70. No. 50. pp. 1223–1225.

It is claimed that the three best known varieties of fungus are the *E. inguinale* of Sabouraud, the *E. interdigitale* of Kaufmann-Wolf and the *E. rubrum* of Castellani. Clinically the three are indistinguishable but all show periods of quietude and activity. The signs and symptoms are always more violent on sweaty feet and secondary infections may mask the underlying condition. Generalization is sometimes seen and the lesions may then simulate pityriasis rosea or a discoid dry eczema. It is suggested that a sympathetic mechanism is involved in the development of the epidermophytides of the hands. Simple microscopy is insufficient to establish the diagnosis ; in the author's view this should always be supported by culture. There has been a great increase in the detected cases during the last few years. This is partly due to greater knowledge of its existence, to the communal type of life seen in sport clubs, etc., and there may also be some actual increase of the prevalence of the fungi in nature owing to some meteorological or atmospheric condition undetected by us, just as climate causes variations in other vegetable fungi in woods, etc., from year to year.

Only about one-quarter of this paper is actually devoted to treatment. The author recommends one or two per cent. iodine in alcohol for chronic cases. Wet dressings under gutta percha help the acute cases. Often one erythema dose of X-rays is successful when it is followed by three weeks of the iodine treatment. As the usual routine, however, he advises bathing of the feet in a 1 in 4,000 aqueous solution of permanganate of potash containing one half per cent. of common salt. All bullae are broken and the feet generally "cleaned up." The following paint is then applied : 20 per cent. of acetone, 2 per cent. of iodine, and 60 per cent. of alcohol, in water. When this

application has dried the feet are dusted with a powder consisting of equal parts of zinc oxide, talc and bismuth subnitrate. A light gauze dressing is then applied. The claim is made that this method produces cure in about three weeks. It is noteworthy that there is no mention whatever of the sterilization of socks, etc.

Sydney Thomson.

Stephens (Frances L.). **Preliminary Laboratory Tests on the Fungicidal Action of Copper Sulphate and Para-Nitrophenol on Dermatophytes.** With a Corollary by Surgeon Lieutenant-Commander P. K. Fraser.—*Jl. Roy. Nav. Med. Serv.* 1941. July. Vol. 27. No. 3. pp. 273–281. [Summary appears also in *Bulletin of Hygiene.*]

Interest in this subject was aroused by the hope of developing a prophylactic bath. The resulting laboratory work may be summarized briefly and although its results are not encouraging there is always the fact that clinical experience often proves more hopeful than might be expected. The arguments on this point are discussed in the corollary by Fraser. It was found that a 2 per cent. aqueous solution of copper sulphate required five hours to kill *Tr. rubrum* and *E. floccosum.* A 5 per cent. solution took four hours to achieve the same result. Thirty minutes' application proved lethal to *E. floccosum* when a 20 per cent. solution was used, but this same solution took one hour to kill *Tr. rubrum.* Using a saturated aqueous solution of paranitrophenol the same differences are seen, thirty minutes being sufficient to kill the one fungus whilst two hours were needed to deal with the Tricophyton. Both were killed in about 15 minutes when this solution was used *in vacuo*, but when the strength of the paranitrophenol was reduced to 1 per cent., 30 to 60 minutes were necessary.

S. T.

Dey (N. C.) & Maplestone (P. A.). *Trichophyton crateriforme* **in India.**—*Indian Med. Gaz.* 1941. July. Vol. 76. No. 7. pp. 410–411. With 4 figs. on 1 plate.

This organism received its present name in 1902 when it was studied by Bodin. Sabouraud wrote the original description, however, when he called it the *Tr. megalosporon endothrix.* The authors of this paper claim that their seven cases constitute the first report of its occurrence in India. All the patients were Anglo-Indian girls, aged between 7 and 13 years, who were members of a boarding school in Calcutta. Each was a case of tinea tonsurans, but all showed one feature which seems to be very important in the clinical diagnosis. The scalp bore a thick layer of greasy scales in which the hair stumps were so embedded that they showed only as small black specks, the "black dot ringworm." The morphology and cultural characters of the fungus are described in detail.

S. T.

Briceño-Iragorry (L.). Nota acerca de dos casos de Tiña Endotrix. [**Two Cases of Infection by** *Tinea endotrix.*]—*Bol. Laboratorio Clinica "Luis Razetti."* Caracas. 1941. Feb. Vol. 1. No. 3. pp. 65–67. With 1 fig.

Till 1939 the forms of *Tinea tonsurans* recorded in Venezuela, states the author, were *T. endotrix*, the parasite being *Microsporum*

felinum. In 1939, Dr. Paul GUERRA reported 11 cases of fungal infection, four of *Trichophyton sabouraudi*, six varieties of *T. tonsurans* and one of *T. rubrum*, the last causing *Eczema marginatum* of Hebra.

Two cases were seen by the author in private practice in 1940, one a girl of five, the other a boy of 10 years. The former presented small patches with ill-defined edge, scaly centre and broken hairs; the condition had been in progress for six months; the latter showed a single patch, "the size of a 5-bolivar-piece," crusted, on the occipital region, also with diffused edge and hairs matted in the scab; it had been noticed for a year.

Culture on Sabouraud's medium gave two types of colony; one large, powdery, with creamy yellow centre, whiter towards the periphery, crateriform in the middle with radiating fissures. The other type was fluffy and downy (duvetosa), white, less powdery and smooth. In the former was abundant sporulation with many conidia and simple or ramifying conidiophores, and very rarely intercalary chlamidospores. In the latter, conidia were less abundant from conidiophores usually simple, terminal or lateral, but with more numerous chlamidospores. The fungus was identified as *Trichophyton tonsurans*, better known as *T. crateriforme* Sabouraud 1902. The latter, in the opinion of CARRIÓN, is merely a variant of the former.

H. H. S.

SHAW (Frederick W.) & REID (J. Douglas). **Fungi and Fungous Diseases.**—*Jl. Lab. & Clin. Med.* 1940. Oct. Vol. 26. No. 1. pp. 256–262. With 3 figs. [18 refs.]

This article is really devoted to three of the more obscure mycotic lesions. It is intended to remind readers of their existence, and so only such points are mentioned as may assist in rapid differential diagnosis. CHROMOBLASTOMYCOSIS affects the skin only and does not appear to invade the other organs. Its warty and nodular appearance demands differentiation from tuberculosis verrucosa cutis, blastomycosis, Madura foot and coccidioidal granuloma. Under the microscope the causative organisms differ from *Blastomyces dermatitidis* by their dark colour and by the absence of budding forms. *Coccidioides immitis* is distinguished by the presence of endospore formation in that fungus. TORULA MENINGITIS, of which there are 64 examples in the literature, is protean in its clinical manifestations. Usually the patient is either quite afebrile or has only a low grade fever. The disease lasts weeks and has been known to persist for a number of years. The c.s.f. shows 100 to 500 cells per cc., lymphocytes predominating. The oval yeast cells are present in it and are Gram-positive and 5–8μ in diameter. Mice and rats are susceptible to this *T. histolytica*, thus being useful in its detection. The more virulent strains show large capsules. There is no known treatment apart from the usual symptomatic measures. SYSTEMIC HISTOPLASMOSIS is caused by *H. capsulatum* but is exceedingly rare. Onset is insidious with weakness and loss of weight. Sweats may occur. There is an irregular fever, an enlargement of the spleen, liver and lymphatic glands. Leucopenia and secondary anaemia are present. The parasite may be found in the cytoplasm of the large endothelial-type cells in the blood. When stained by Wright's method the fungus shows as bluish oval cells 2–4μ in diameter, each being surrounded by a clear

capsule-like substance. Under the appropriate conditions cultures also show a mycelial type of growth. The most suitable experimental animals are guineapigs. Nothing so far is known about treatment, as only two cases have been diagnosed during life, and then only very late in the course of the disease. *S. T.*

SMITH (Leslie M.). **Blastomycosis and the Blastomycosis-like Infections.**—*Jl. Amer. Med. Assoc.* 1941. Jan. 18. Vol. 116. No. 3. pp. 200–204. With 5 figs. [18 refs]

The author prefers " to reserve the name blastomycosis for lesions caused by the species of fungus described by Gilchrist and named *Blastomyces dermatitidis* and to apply appropr ate names to the other somewhat similar diseases caused by other species of fungi," including the mycotic granulomas in which yeast-like cells are found. He insists that clinical characteristics, although suggestive, are usually not sufficient for accurate diagnosis, and that identification of the organism must be made as soon as possible. In most cases study of the cultures is necessary. Intracutaneous tests with fungus antigens assist but are not absolutely specific. Geographical distribution may help a little. " The extreme adenopathy of paracoccidioidal granuloma suggesting Hodgkin's disease, the marked fungating character of chromomycosis, the polypoid tumours of rhinosporidiosis, the gelatinous contents of torular abscesses and the kala-azar-like syndrome of histoplasmosis are distinguishing clinical features " in many cases. The verrucous surface and miliary abscesses of blastomycosis have also been imitated in superficial coccidioidal granuloma and deep moniliasis. Among the other diseases here considered are sporotrichosis and scopulariopsosis. The paper contains many useful tables showing the comparative features, clinical, pathological and mycological. *S. T.*

BUSH (J. D.). **Severe Generalized Blastomycetic Dermatitis. Report of a Case.**—*Arch. Dermat. & Syph.* 1941. Mar. Vol. 43. No. 3. pp. 485–490. With 4 figs.

An Alabama negro, aged 48, gave a total history of only four months. The eruption then started as dry, white, elevated patches on the forearms. The typical warty lesions developed later and also appeared on the body in scattered areas, whilst the face became thickly involved. This paper is chiefly concerned with the question of treatment. Iodide of potash was given in doses of 360 grains daily. At the same time the U.S.P. compound solution of iodine was administered intravenously. At first 15 minims were given daily, later this dose was increased to 30 minims and was continued for six weeks. One gramme of sodium thiosulphate was mixed with each dose, a suggestion originally made by RAVAUT, who hoped to preserve the veins and prevent clotting by this means. X-rays were also given but the doses are not noted. Great improvement was seen after seven weeks, so that only the iodide of potash was thereafter given until three months had elapsed after his admission to hospital. By then cure seemed apparent and in fact the man was still quite well when seen two years later. *S. T.*

Weidman (Fred D.) & Rosenthal (L. H.). **Chromoblastomycosis : a New and Important Blastomycosis in North America. Report of a Case in Philadelphia.**—*Arch. Dermat. & Syph.* 1941. Jan. Vol. 43. No. 1. pp. 62–82. With 5 figs. [34 refs.]

"It is the main purpose of this paper to publicize the rapid expansion of the geographic distribution of chromoblastomycosis and to indicate the enlarging scope of the morbid anatomic changes. . . . There is promise that the range in gross tissue reaction will eventually compare with that of tuberculosis, syphilis and other members of the group of specific infectious granulomas." The case, seen in Philadelphia, was that of a negress, aged 44 years, whose disease began some 10 years earlier. When first seen there were three fungating lesions on the left ankle, with abscesses in their centres. No real verrucous changes were seen. Treatment with iodine internally, and with radiotherapy, produced great improvement. Diffuse local nodes were subsequently dispersed by iodide of potash, so that some five years later there was a pigmented patch, with but two small active areas, which clinically suggested a late nodular syphiloderm.

Beautiful photographs illustrate the histological and cultural reports, *Fonsecaea* [*Hormodendron*] *pedrosoi* having been isolated. The changes seen extend from mere infiltration with erythematosquamous patches, through discrete gummatous nodules to exaggerated verrucosities. The authors discuss the history of the disease and its geographical distribution very fully. The dermatologist must be conscious that this infection must now be reckoned among the distinct possibilities in granulomas of undetermined nature, as well as in verrucous dermatoses in general. It must also be realized that whilst the condition has been confined to one of the lower extremities in most known cases, exceptions have been discovered with increasing frequency in recent years, *e.g.* the hand is not uncommonly affected, whilst lesions have been detected on the arms, buttocks, face and neck. *S. T.*

Emmons (C. W.), Hailey (Howard) & Hailey (Hugh). **Chromoblastomycosis. Report of the Sixth Case from Continental United States.**—*Jl. Amer. Med. Assoc.* 1941. Jan. 4. Vol. 116. No. 1. pp. 25–28. With 5 figs. [13 refs.]

The authors describe this the sixth case seen in the U.S.A., the patient being a man 68 years of age and a native of Atlanta. The lesion was said to be of three months' duration, and was situated on the back of the left wrist, where it covered an area four cm. in diameter. The raised bluish-red patch was boggy to the touch and bore multiple points of discharge. Cultures proved the organism to be *Hormodendron pedrosoi*, the description of which is supported by good photographs. It is claimed that the man was cured after three months' treatment, but his subsequent death in an accident rendered prolonged observation impossible. On the first day 150 R units of X-rays were administered, this being followed a fortnight later by a further 75 R units. Iodide of potash was given as a saturated solution, starting with thirty drops three times a day after meals. Thereafter each dose was increased by one minim daily, so that 20 days later the man was taking 50 minims three times a day. Reduction of the

dose was then carried out along the same lines, so that in three weeks time he was back on half a drachm three times a day, which dose was then continued until the three months were complete. *S. T.*

Niño (Flavio L.). Micetoma podal maduromicótico con granos blancos por "Monosporium Apiospermum" en la República Argentina. (Estudio micológico de una observación.) [**Madura Foot due to** *Monosporium apiospermum* **in the Argentine.**]—*Bol. Inst. Clin. Quirúrg.* Buenos Aires. 1941. June–July. Vol. 17. No. 141. pp. 483–509. With 23 figs. [43 refs.]

The patient was an unmarried man of 26 years of age, who a year before coming under the author's observation had punctured his foot with a pine needle. A typical fungoid condition followed, with extension to the deeper structures and sinuses discharging white granules. There is nothing particular to remark about the clinical condition, except perhaps its rapidity of development. It is, however, described in great detail by Professor Niño, because it is the first case of pedal maduromycosis with white grains to be recorded in the country, and the causative fungus has not previously been known to cause disease in the Argentine. The article is excellently illustrated with photographs of the foot, and with X-ray reproductions, together with photomicrographs demonstrating the histological changes and cultures of the fungus on Sabouraud's glucose medium. *H. H. S.*

Costa (Oswaldo) & Junqueira (Moacyr A.). Mycetoma podal. Observação clinica de um caso. [**A Case of** *Mycetoma pedis.*]—*Brasil-Medico.* 1941. May 10. Vol. 55. No. 19. pp. 333–335. With 5 figs. English summary (2 lines).

This case is placed on record because the disease is said to be rare in Minas Geraes; this is the fourth to be reported. The patient was a man of 52 years who noticed the early stages—a small, painless swelling the size of a millet seed, beneath the skin. This increased very slowly and when seen by the authors there was swelling involving the whole foot, with sinuses discharging whitish-yellow granules. Radiological examination showed rarefaction of the os calcis, astragalus and cuboid. *H. H. S.*

Almeida (F.) & Barbosa (F. A. Simões). Contribuçao para o estudo de "Cephalosporium recifei". [**Description of** *C. recifei.*]—*Arquivos do Inst. Biol.* São Paulo. 1940. Vol. 11. pp. 1–4. With 5 figs. on 2 plates. English summary.

"The authors, following their studies on maduromycosis in Brasil, describe for better documentation the *Cephalosporium recifei* Leão and Lobo. They found a characteristic appearance on Czapek's medium.

"The fungus was obtained from a case of mycetoma in Pernambuco, and it is the first case of mycetoma produced by a specimen of this genus registered in medical literature."

DANGERFIELD (L. F.) & GEAR (James). **Sporotrichosis among Miners on the Witwatersrand Gold Mines.**—*South African Med. Jl.* 1941. Apr. 12. Vol. 15. No. 7. pp. 128–131. With 2 figs.

Some 74 cases are analysed in this paper. Only six cases were seen in European miners, the remainder occurring in natives. From one mine there came 17 patients, most of whom worked in one shaft on timbering. The rest all worked in one shaft of a second mine, but at very different levels. It cannot be said that any particular type of work was dominant as the infection appeared in some who were lashing, timbering, machining, washing rock and even in some transport men. The disease usually developed at the site of known injury; thus 23 of the 57 men from the second mine gave a definite story of antecedent trauma. This was mostly chafing on rock, but a few told of splinters from the timber. The incubation period varied from three days to three weeks, the primary lesion usually being on the forearm or wrist. There it developed as a small granulomatous ulcer which later became surrounded by minute nodes. These gradually became confluent and then in turn broke down to make the edge still more irregular. Occasionally multiple primary foci were seen. The secondary deposits appeared one or two weeks after the primary site had become evident, occurring as small hard nodules along the course of the draining lymphatics. These in turn then broke down. Retrograde lymphatic spread was seen occasionally. Some confusion might be caused by the adenitis resulting from secondary pyogenic infection. Spontaneous healing is known but the authors produced cure by intensive doses of iodide of potash, reaching one drachm three times a day by the third day of treatment. This was continued for three weeks. All attempts to trace the sources of infection were unsuccessful. *S. T.*

LAFFER (Norman Callender). **A Note on *Saccharomyces fragilis* Jorgensen associated with Pathologic Conditions in Human Beings.**—*Jl. Lab. & Clin. Med.* 1940. Nov. Vol. 26. No. 2. pp. 294–296.

This report is solely concerned with an organism isolated by Miller in 1835 and classified by him as *Monilia pseudotropicalis* Castellani. Diddens and Lodder considered this to be an imperfect stage of *Saccharomyces fragilis* Jorgensen. These confusing results are always liable to occur as it is difficult to stimulate ascospore production in some strains. The patient from whom this particular strain was isolated had an acute follicular tonsillitis with all the usual systemic disturbance. Recovery occurred after the administration of diphtheria antitoxin. The first case in which the organism was found had a tonsillitis too, but the only other report claimed its isolation from the "lung of a tuberculous patient." The fungus is actually by no means rare and has been found in cream from Illinois, milk from Copenhagen and from Switzerland, in *yoghurt* from Germany and *matzoon* from Armenia. The paper contains very full cultural, morphological and biochemical details. The findings confirm the work of DIDDENS and LODDER. *S. T.*

CONANT (Norman F.). **A Cultural Study of the Life-Cycle of *Histoplasma capsulatum* Darling 1906.**—*Jl. Bacteriology.* 1941. May. Vol. 41. No. 5. pp. 563–574. With 3 plates. [28 refs.]

"1. A strain of *Histoplasma capsulatum* from a fatal case of histoplasmosis in a three-months old infant is studied.

" 2. The saprophytic filamentous form developed on Sabouraud's glucose agar at room temperature is characterized by large tuberculate chlamydospores, not asci, as proven by appropriate staining methods.

" 3. The filamentous form is converted to the yeast-like tissue form without the use of animal inoculation by cultivation on sealed blood agar slants at 37°C.

" 4. From a cultural study of the complete life-cycle of *Histoplasma capsulatum* it is shown that the fungus should be placed in the Moniliaceae of the Fungi Imperfecti."

VAN PERNIS (Paul A.), BENSON (Miriam E.) & HOLINGER (Paul H.). **Specific Cutaneous Reactions with Histoplasmosis. Preliminary Report of Another Case.**—*Jl. Amer. Med. Assoc.* 1941. Aug. 9. Vol. 117. No. 6. pp. 436–437.

A man, 63 years of age, suffered from hoarseness, loss of weight and abdominal pains. Examination of the larynx showed a polypoid growth on the cord and involvement of other structures. Tissue removed by biopsy revealed an infection with *Histoplasma capsulatum*. Cultures of the organism were obtained and mice were infected. Specific immediate and delayed skin reactions were produced both in the patient and in infected mice by injection of filtrates from broth cultures. The specific substance in the filtrates was precipitated by acetone and was readily soluble in saline solutions. In spite of numerous remedies administered with a view to controlling the disease, it progressed steadily, the patient dying six months after the diagnosis of histoplasmosis had been made. *C. M. Wenyon.*

BOLETÍN DE LA OFICINA SANITARIA PANAMERICANA. 1941. Mar. Vol. 20. No. 3. pp. 215–219. English summary. Algunos datos sobre el carate en Venezuela. [**Pinta in Venezuela.**]

" The first medical writers to study carate in Venezuela were the Freites and the Pinedas ; they were followed by Padilla (1908), Medina Jiménez (1916), Vagas (1918), Iriarte, and Briceño Rossi. According to the last two investigators, carate is found in the States of Anzoátegui, Bolívar, Barinas, Miranda, Lara, Portuguesa, and Zulia and the Territories of Delta Amacuro and Amazonas. Recently a scientific expedition to study the disease and its etiology in the foci Guatire and El Consejo, States of Miranda and Aragua, composed of Drs. Fernández, Vegas, O'Dally, Guerra, Pifano, Iriarte and Briceño and the foreign scientists Brumpt (Jr. and Sr.), Jaffe, Mayer, and Sánchez Covisa, was organized by the National Institute of Health of Venezuela. These investigators found the *treponema* described by Cuban writers, in untreated Venezuelan cases of the lead- or bluish-coloured type of carate ; the organism was relatively rigid, with regular, narrow spirals (12 to 15 microns wide) and its motility decreased about 20 minutes after the specimen was taken. With the Giemsa or Fontana stain, it was very similar to *T. pallidum* and *T. pertenue*. Inoculation in guineapigs, rabbits and rats was negative. Over 50 per cent. of the cases seen had gland swellings resembling those of syphilis. The typical colour of the carate lesion was lead grey, often with bluish tones ; sometimes almost black. The achromatic patches occasionally showed a pinkish tinge. It was felt that there were two kinds of decoloration : one an active type, modified by treatment ; the other residual. In the active

type the hair retained its normal color ; in the latter it became white. No hyperkeratotic or peeling lesions were seen. Bradycardia was present in a high percentage of cases, and slight blood changes (lymphocytosis and eosinophilia) were seen in some. It was noted that pigmentation was not limited to the basal layer of the skin, but extended into the prickle layer ; there were many chromatophores in the dermis. In the epidermis, atrophy of the mucous body, often marked, was observed ; in some parts there was a pronounced morphologic change, with disorganization of the basal layer and irregular arrangement of the remaining cells ; in some places heterotopic mitoses were seen, with infiltration of dermic cells (sometimes lichenoid in appearance) into intracellular spaces."

León y Blanco (Francisco). Estudio epidemiologico del mal del pinto en una pequeña aldea del estado de Guerrero (Mexico). [**Epidemiological Study of Pinta in a Small Village in Guerrero.**]—*Rev. Med. Trop. y Parasit.* Habana. 1940. July–Aug. Vol. 6. No. 4. pp. 185–200. [16 refs.]

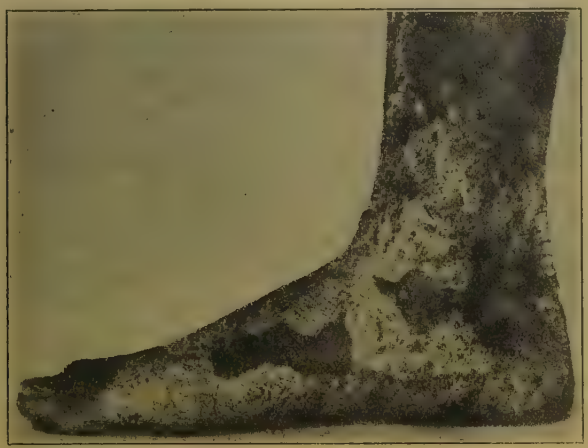
The village referred to is Tecomatlán, which lies in the valley of the Balsas river, which runs between Guerrero and Michoacan. The inhabitants altogether number only 234, and of these 71 (30·3 per cent.) present the dyschromic stage of mal del pinto, six are in the general dissemination stage, and seven show merely the initial lesions, together 84, or 35·9 per cent., of the inhabitants. Forty-three stated that they had had a local rash, or pintid [" empeine " is used for a cutaneous condition, such as " ringworm," for example] before the maculae appeared, 20 had not, while another eight " did not know." As regards sex there was little difference, 46 were male, 38 female [but the relative numbers among the inhabitants are not stated]. A list of the inhabitants is given in families, with a note as to which members were attacked. Whether the disease is contracted by contact or by vector is not certain ; there is no proof of the latter, though the former has undoubtedly been shown to be possible experimentally. *H. H. S.*

Carrión (A. L.), Ruiz Nazario (R.) & Hernandez Morales (F.). Mal del pinto en Puerto Rico. [**Pinta in Porto Rico.**]—*Bol. Asoc. Med. de Puerto Rico.* 1941. Mar. Vol. 33. No. 3. pp. 104–106.

The patient was a woman of 32 years, a native of Patillas, Porto Rico, who complained of certain discoloured spots on the skin which first began to appear five years before. Apart from these spots she seemed to be in excellent health. The spots or blotches were of varied sizes and were present on the face, neck, shoulders and arms ; some had slightly raised edges. Scrapings revealed no fungi. Wassermann and Kahn tests gave negative results. Tissue taken by biopsy and stained by Levaditi's method showed no spirochaetes. Eleven months later characteristic *Spirochaeta herrejoni* were seen by dark ground examination of the lymph obtained by scarification of the skin of the parts affected. Salvarsan was injected but was badly tolerated and had to be stopped after four doses and bismuth salicylate was substituted, and the blotches had greatly improved when after six weeks the patient ceased to attend and passed from the authors' observation. The disease is probably not very rare in Porto Rico. *H. H. S.*

León y Blanco (Francisco). Las queratosis palmares y plantares en el mal del pinto. [**Palmar and Plantar Keratosis in Pinta.**]—*Rev. Med. Trop. y Parasit.* Habana. 1940. July–Aug. Vol. 6. No. 4. pp. 167–184. With 11 figs.

Keratodermia is a late manifestation of pinta and is always accompanied by widespread dyschromia. It is characteristic in the second or generalization stage. The affected surface is irregular and friable (desmenuzada) and covered with adherent greasy scales, and showing deep cracks perhaps exuding bloodstained serum in which *Spirochaeta herrejoni* may be seen. In the foot the part from the heel to the metatarso-phalangeal prominence is usually invaded, but the lesion may



Keratodermia in Pinta.

[Reproduced from *Revista de Medicina Tropical y Parasitologia.*]

extend to the toes ; the heel and midplantar region are always more affected than the rest of the sole. It may extend over the ankles and up the leg like a sock, or halfway up the arms ; patches may show a yellow or a silvery pigmentation. One or both sides may be involved ; if both, one is more affected than the other. Diagnosis has to be made from " symptomatic keratodermia," from syphilis and from yaws, and can usually be made by noticing the presence of the widespread dyschromias characteristic of mal del pinto.

The author believes that in Cuba late yaws and syphilis lesions are included under the name Pinta, though careful examination should enable one to make the distinction. *H. H. S.*

León (Luis A.). El mal del pinto en el Ecuador. [**Pinta in Ecuador.**]—*Rev. Med. Trop. y Parasit.* Habana. 1940. Sept.-Dec. Vol. 6. Nos. 5 & 6. pp. 253–276. With 7 figs. Also in *Acta Med.* Rio de Janeiro. 1941. July. Vol. 8. No. 1. pp. 3–27. With 7 figs. on 4 plates. English summary (3 lines).

Ramirez (E.) & Rivero (M. D.). Estudio comparativo de las reacciones de Wassermann, Kahn y Proske en enfermos de mal del pinto. [**The Wassermann, Kahn and Proske Reactions in Pinta.**]—*Rev. Inst. de Salubridad y Enfermedad. Trop.* Mexico. 1940. Dec. Vol. 1. No. 4. pp. 311–318.

The Wassermann and Kahn reactions are matters of general knowledge, the Proske tyrosin reaction is less well known and calls for description. The materials used are :—

1. A solution of sodium sulphate, 14 per cent. Seventy gm. of the anhydrous salt are dissolved in 300 cc. of freshly distilled water, and made up to 500 cc. at 37°C. This is kept in a thermostat at 37°C.

2. Solution 5/N NaOH.

3. Tyrosin solution, made by dissolving 200 mgm. or pure tyrosin in 100 cc. of decinormal HCl.

4. Folin-Ciocalteau's reagent. In a 1,000 cc. receptacle is placed 100 gm. of sodium molybdate, 700 cc. of water, 50 cc. of 85 per cent. phosphoric acid and 100 cc. of concentrated HCl. Allow to stand for 10 hours, then add 1,500 gm. $CuSO_4$, 50 cc. water and a few drops of bromine. Boil for 15 minutes to drive off excess of bromine, cool, make up to 1,000 cc. and filter. There should be no green coloration.

Method : In a test-tube are placed 3 cc. of No. 1, then 0·1 cc. of blood serum (carefully measured), invert the tube 10–12 times, avoiding frothing, and place at 37°C. for three hours. Centrifuge at 1,500 r.p.m. for 10 minutes, decant the supernatant fluid, wash the precipitate with No. 1 and centrifuge twice to remove all traces of albumen and pseudo-globulin. Add 1·75 cc. water and 0·1 cc. of No. 2. Place in water-bath kept at boiling point for 10 minutes, cool and add 0·15 cc. of No. 4. Shake gently and within 10 minutes read off the colour, using the Pulfrich photometer and compare it as found in each serum tested with the absorption curves plotted with standard tyrosin solutions. This curve is made by placing 2 cc. of solution No. 3 in a 20 cc. graduated tube, adding 5 cc. water and 1 cc. of No. 2, warm in a boiling water-bath for 10 minutes, cool and add 1·5 cc. of No. 4, make up to 20 cc. with water. A series is put up as follows with increasing amounts of water and diminishing of standard solution :—

Tube	1	2	3	4	5	6	7	8	9	10
Water	0	0·2	0·4	0·6	0·8	1·0	1·2	1·4	1·6	1·8
Standard solution ...	2	1·8	1·6	1·4	1·2	1·0	0·8	0·6	0·4	0·2
Tyrosin index	100	90	80	70	60	50	40	30	20	10

The results in 100 cases are given in a series of three tables, and may be summed up thus :—

1. Patients with W.R. and Kahn negative but showing initial lesions of pinta have an average tyrosin index of 97·7, with minimum 60 and maximum 148 (3 cases).

2. Those with W.R. negative, but Kahn + to +++, and showing " piantids " give an average of 69, and limits of 36 and 116 (9 cases).

3. Those with classical pinta (leucomelanodermia), with W.R. negative, Kahn positive have an average of 139 and limits of 53 and 240 (17 cases).

4. Those with W.R. weak or moderately positive, Kahn distinctly positive, have average 105, with limits of 60 and 189 (10 cases).

5. Those with pintids, and W.R. and Kahn both positive have an average of 155·6 with limits of 73 and 368.

[The minima and maxima in these groups seem widely separated.]

The author concludes that the earliest serum reaction to appear in this disease is that of Kahn, the Wassermann comes later, but in the florid state both are positive. As soon as the Kahn shows positive the tyrosin euglobulin index tends to mount, and it increases as the other reactions become frankly positive, but the tyrosin index is no guide to, *i.e.* does not run parallel with, the extent of the maculae, nor has the total serum albumen any relation to the three reactions. *H. H. S.*

León y Blanco (Francisco). Las reacciones de Bordet-Wassermann y de Kahn en el periodo secundario del mal del pinto. [**Wassermann and Kahn Reactions in Pinta Patients.**]—*Rev. Med. Trop. y Parasit.* Habana. 1940. July–Aug. Vol. 6. No. 4. pp. 201–205. [10 refs.]

Serological tests have been carried out with the blood of 107 patients in the second stage, that of generalized or widespread dissemination, of mal del pinto. In all 107 the Kahn test was made, and in 94 the Wassermann. Of the former, 95 were positive and 12 negative, or 88·7 and 11·2 per cent. respectively. Of the latter 81 were positive (86·1 per cent.) and 13 (13·8) negative. In six cases the W.R. was negative though the Kahn gave a positive, and in some of those giving a positive to both, that to the Kahn was the more definite and intense. The intensity of reaction was variable ; in general it was more marked the more advanced the condition, but this did not always hold good.

H. H. S.

Escobar (J. J.). **Blue Dermatosis of People of Chillos Plateau.**—*Rev. de Higiene.* Bogotá. 1940. May–June. Vol. 21. p. 38. [Summarized in *Jl. Amer. Med. Assoc.* 1941. July 19. Vol. 117. No. 3. p. 231.]

"Escobar describes a new type of chronic dermatosis among people who lived in the Colombian Chillos Plateau for a long time. The prominent lesions are squamous dermatitis on areas of dark blue pigmentation of the skin, alternating with areas of achromia and dyschromia, exfoliation and ulcerations of mucous membranes, especially those of lips and lids. Areas of normal pigmentation, such as those of the areola of the nipple and of the scrotum, are not involved. The bare parts of the body are more frequently involved than the protected parts. The sensitivity of the skin is well preserved. The lesions are not pruriginous. The morphologic blood picture is normal for persons of that region. The incidence is the same for peoples of different race, age and sex. Alopecia and general adenopathy are commonly present. The removed ganglions contain fine grains of pigment. Serologic tests for syphilis give strongly positive results in all cases. The patients, however, have neither a history nor clinical symptoms of syphilis. The ulcers follow a slow course and do not heal spontaneously. Spirochetes can be isolated from the skin, lesions, ulcers and ganglions. It is a new species of Spirochaeta, different from *Spirochaeta pallida* and *Spirochaeta carateum*. Administration of two doses of 0·3 and 0·4 Gm.

of arsphenamine, respectively, results in disappearance of the spirochetes and cure of the lesions. The disease must be differentiated from vitiligo, leprosy, syphilis and caraate."

SILVA (Flaviano). Contribuição ao estudo do purú-purú. [**Contribution to the Study of Purú-Purú.**]—*Brasil-Medico.* 1940. June 22. Vol. 54. No. 25. pp. 425–433. With 6 figs.

Purú-purú is closely allied to, if not identical with, pinta [it must not be confused with purru ; a synonym of yaws in Malaya]. Purú-purú (or curú-curú) is common among the natives of the Amazon and is characterized by patches ash-coloured or more darkly pigmented and in other parts achromic, like vitiligo. It has many synonyms—pityriasis nigra with depigmented centre, mal azal (blue disease) of Bolivia, cara in Peru, querica in Panama and Honduras.

In the early stages the parts affected are flat or slightly raised, scaly and itching ; later they become, in parts at least, depigmented starting from the centre, and itching ceases. Occasionally the patches are hyperchromic from the start. Pathologically, the stratum corneum is thickened, the melanin pigment layer increased, the walls of the papillary and subpapillary vessels thickened and there is marked infiltration with lymph- and plasma-cells. The palms and soles show much hyperkeratosis.

The disease rarely affects white people, unless they are living with the Indians. All ages are affected, but rarely any under 4–5 years of age. The author describes two cases, one in girl of 15 and one in a man of 50 years. He discusses the causation under the heads of deficiency disease, mycotic infection (some authorities ascribe it to an aspergillus), spirochaete (*Sp. herrejoni* as in pinta) because the W.R. is positive in these patients, but reaches no very definite conclusions. Next, he considers the question of diagnosis, discussing its differentiation from vitiligo, leprosy, syphilis, yaws, pityriasis versicolor, tinea alba and tinea nigra, tokelau or tinea imbricata, chimberé (an epidermomycosis of Bolivia). Treatment of various kinds has been recommended : iodine, salicylic acid, yellow oxide of mercury, chrysarobin and the like as parasiticides or fungicides, but MATTA of Manaos states that arsenobenzol is the best and claims to have obtained cures for many years from its use. *H. H. S.*

LEVIN (Oscar L.) & BEHRMAN (Howard T.). **Coral Dermatitis.**—*Arch. Dermat. & Syph.* 1941. Oct. Vol. 44. No. 4. pp. 600–603. With 1 fig. [Summary appears also in *Bulletin of Hygiene.*]

Direct injuries from coral fragments and those due to stinging coral animals must be distinguished. Cuts of the skin from coral have often been noticed to cause very indolent lesions, and the delay in healing has been attributed to the constant contact with salt water. A mere scratch, if ignored, may in a few days become an ulcer with a sloughing base and red surrounding skin, and even if the scratch is immediately washed with saline solution and painted with Tr. iodi, a tender red indurated area may persist for a week or longer.

Injury may, however, follow mere contact and is then due to one of the Anthozoa, a coral polyp or sea-anemone ; the Actinia genus has

" lasso " cells, tubular cells which evert themselves and end in a harpoon-like structure. A mollusc or crab falling on the flower is at once poisoned by the lassos and unable to offer resistance.

The case is reported of a man of 43 years, in the West Indies, who, diving for coral, picked up a piece and felt a stinging of the forearm. Within a very few minutes, watery beads appeared from clear fluid oozing from the skin which itself became red, oedematous and itchy. In less than 24 hours a slough was discharged leaving an ulcer two inches in diameter, which did not heal for several months and left a thick scar. The same coral, *Madapora palmata*, can be broken by the hand without harm, because, so it seems, the palmar epidermis is too thick for penetration of the stinging cell.

It is to be noted that this form of dermatitis is primary and not preceded by a break in the skin. *H. H. S.*

MALARIA.

Public Health Reports. 1940. Oct. 4. Vol. 55. No. 40. pp. 1801–1809.—**A Brief Review of Needed Research in Malaria.**

This is a short report by a group of United States malariologists who met to consider some fundamental aspects of malaria research. It is particularly concerned with the large and important gaps in present knowledge of malaria, and with suggestions as to constructive efforts that might help to fill in those gaps. Suggested lines of investigation concern chemotherapy, the biology and physiology of the parasite, immunological studies, and the bionomics and ecology of anophelines. There is " a compelling necessity for increasing knowledge of the prophylaxis and treatment of malaria, as well as the control of anopheline production." *Norman White.*

Bocalandro (Carlos A.) & Wilde (Hugo J.). La lucha contra el paludismo. Acción de la Cruz Roja. [**Antimalaria Campaign : Rôle of the Red Cross.**]—*Rev. Sanidad Militar.* Buenos Aires. 1941. Jan. Vol. 40. No. 1. pp. 21–26.

This paper describes in general terms the distribution of malaria in the Argentine. The disease is endemic in the northern part of the country, over an area of some 120,000 square kilometres, inhabited by 850,000 people. The most important, if not the sole, vector is *A. pseudopunctipennis*. Other anophelines, for example *A. argyritarsis*, are found in greater abundance, but man has but little attraction for this latter species, which is very rarely found in human habitations. After a description of antimalaria measures in general the authors reach the conclusion that very few of them are practicable in existing conditions. *N. W.*

GARCIA (Eusebio Y.). **A *Plasmodium ovale*-like Parasite in the Blood of a Native Filipino.**—*Acta Med. Philippina.* 1941. Jan.–Mar. Vol. 2. No. 3. pp. 341–349. With 2 plates (1 coloured). [11 refs.]

The paper gives a description of a malarial parasite of the *Plasmodium ovale* type, which was discovered in the blood of an eleven-year-old Filipino in Manila. The parasite showed all the main features of *P. ovale*—tendency to oval form, fimbriation of margin of the red blood corpuscle, Schüffner's dots and their early appearance after infection of the corpuscle, failure of corpuscle to enlarge, and merozoite number of 8 to 12. The discovery of the parasite in Manila is of interest in the light of CRAIG'S description of a similar form in 1900 in the U.S.A. in the blood of an American soldier returned from service in the Philippines. Craig later identified his parasite with one described by EMIN in 1914 as *P. vivax* var. *minuta* and with the form named *P. ovale* by STEPHENS in 1922. It seems probable that all three forms are actually *P. ovale* and that the author has re-discovered the parasite in the Philippines after a lapse of 40 years. The paper is illustrated by a plate of microphotographs and another of coloured drawings of the parasite. *C. M. Wenyon.*

KHODUKIN (N.) & SHTERNGOL'D (E.). **On the Resistance to Cold of Some *Anopheles*.**—*Acta Univ. Asiae Med.* Tashkent. 1938. (8, Zool.) No. 45. 11 pp. With 3 graphs. [In Russian. English summary.] [Summarized in *Rev. Applied Entom.* Ser. B. 1941. Sept. Vol. 29. Pt. 9. p. 141.]

" Laboratory investigations were carried out in Tashkent on the resistance to cold of females of *Anopheles maculipennis* var. *sacharovi*, Favr., *A. superpictus*, Grassi, and *A. pulcherrimus*, Theo. The experimental technique is described, and the results are shown in tables. Previous work in Russia has shown that cold-resistance in insects depends on the amount of fat present in the body, the degree of nutrition and the quantity of fluid in the body that freezes. The last of these factors is largely dependent on the first two. The temperature at which the fluid freezes cannot be taken as an accurate index of cold-resistance, since it is dependent on all three factors. The authors' investigations showed that although females of both *superpictus* and *pulcherrimus* froze at −7·8°C. [17·96°F.] and the percentage of fluid in them that froze was almost the same (24·1 and 24·6, respectively), the percentages of fat in them were 73 and 35 ; and that although the percentages of fat in females of *sacharovi* and *superpictus* were of the same order (78 and 73), the temperatures at which the mosquitos froze were −18°C. [−0·4°F.] and −7·8°C. and the percentages of fluid that froze were 63·5 and 24·1, respectively. Two of 12 females of *sacharovi* with a developed fat-body survived exposure for 30 hours to a temperature of −20°C. [−4°F.], but all those of *superpictus* amd *pulcherrimus* died after exposure for 17 and 20 hours to −9·5 and −7°C. [14·9 and 19·4°F.], respectively.

" In Tashkent, females of *A. m. sacharovi* usually hibernate in buildings in which the temperature does not fall below −7°C., and recent observations indicate that, in inhabited localities, those of *A. superpictus* usually select similar hibernation quarters. There is therefore

unlikely to be any mass mortality among these mosquitos in winter. *A. pulcherrimus* does not hibernate in the adult stage.

" In experiments in which eggs of *A. pulcherrimus*, *A. hyrcanus*, Pall., and *A. m. sacharovi* were kept for 16 hours at −4°C. [24·8°F.] those of *sacharovi* did not hatch, whereas those of the other two did so after 48 and 24 hours, respectively. In the controls, the eggs of these mosquitos hatched in 24, 24 and 32 hours, respectively."

RUSSELL (Paul F.) & MOHAN (Badri Nath). **An Insectary Colony of *A. stephensi mysorensis*.**—*Indian Med. Gaz.* 1941. Apr. Vol. 76. No. 4. pp. 219–220.

In India there are two distinct types of *Anopheles stephensi*, differing in egg-measurements and several biological points. The type form is very easy to rear in cages for an indefinite number of generations; var. *mysorensis* has proved impossible to rear in cages.

The authors find that the difficulty in breeding var. *mysorensis* does not arise (as it does in certain races of *A. maculipennis*) from inability to copulate in cages, but from the female's failure to lay eggs. If the female is gently stunned and then thrown upon the surface of water she will generally lay eggs forthwith. *P. A. Buxton.*

TOUMANOFF (C.). Les " Black Spores " de Ross et la " dégénérescence brune " des microfilaires chez les moustiques, conception nouvelle sur leur nature et origine possibles. Considérations sur la " chitinisation " défensive chez les insectes. [**New Views on " Black Spores " and " Brown Degenerescence " of Microfilaria in Mosquitoes.**]—*Rev. Méd. Française d'Extrême-Orient.* 1940. Apr.–May. No. 4–5. pp. 173–197. With 10 figs. [26 refs.]

The author reviews the various theories which have been advanced in explanation of the " black spores " which are encountered when mosquito dissections for possible malarial infections are carried out. He admits that they occur only in mosquitoes infected with malaria, and that they are the result of changes which take place within the oöcyst. These changes may occur before sporozoites have been formed, when the dark bodies will be rounded structures, or after sporozoites have developed, when they are banana shaped. In either case he disagrees with the view that the dark substance is chitin. He considers rather that it is melanin or a complex of this substance and chromolipoid, which results from the oxidation of protein degradation substances (polypeptides to tyrosin) by tyrosinase and the auto-oxidation of lipoids during the course of degenerative changes within the oöcyst. In support of this oxidation hypothesis is the observation of Bruce MAYNE that oöcysts containing " black spores " are always closely associated with a branch of the mosquitoes' tracheal system. A similar explanation is advanced for the brown pigment which forms around degenerating filariae in the organs of mosquitoes. It has been supposed, as in the case of " black spores " that this pigment is chitin, but the author finds that there is no evidence of this. Furthermore, he expresses the opinion that the so-called chitinous deposits by which insects in general are able to protect themselves against invading organisms are not of this nature but are again, as in the case of " black spores," merely pigments resulting from the oxidation of degenerating

proteids and have no relation to protective mechanisms which in insects are represented by the accumulation of phagocytes at the sites of invasion. *C. M. W.*

Ou (Teishun). Zum Studium ueber die Funktion der Retikuloendothelialsystems bei Malaria. [**The Function of the Reticulo-Endothelial System in Malaria.**]—*Taiwan Igakkai Zassi* (*Jl. Med. Assoc. Formosa*). 1941. Apr. Vol. 40. No. 4. [In Japanese pp. 770–775. [13 refs.] German summary p. 776.]

After the removal of 5 cc. of blood from the vein of one arm, 10 cc. of a 1 per cent. solution of Congo Red are injected into the same vein. Three minutes and one hour later 5 cc. of blood are taken from the other arm. The sera are separated and photometer readings are taken, the reading from the first blood (taken before the injection) acting as control ; the concentration of the dye in the 60-minute specimen compared with that in the 3-minute specimen is a measure of the capacity of the reticulo-endothelial system to take up the dye. The normal index is regarded as between 60 and 73 per cent. ; in 10 cases of acute malaria the index was from 62·3 to 87·4 per cent., and in 10 cases of chronic malaria was from 56·5 to 85·8 per cent. After treatment the index tends to become normal. *C. W.*

Coggeshall (L. T.). **The Complement Fixation Reaction as a Diagnostic Aid in Malaria.**—Reprinted from *Proc. Indiana Acad. Sci.* 1941. Vol. 50. pp. 53–55.

The need for improved methods in diagnosis, especially in chronic malaria, is self-evident. So far complement-fixation has met with little success ; the chief difficulty being lack of a satisfactory source of malaria parasites as an antigen.

A malarial infection (*P. knowlesi*), which is so highly virulent for *cynomolgus* monkeys, furnishes abundant quantities of antigen which binds the complement in the serum of chronic *vivax*, or *falciparum* malaria [see this *Bulletin*, 1939, Vol. 36, p. 405].

The antigen was prepared from parasitized red cells obtained from *rhesus* monkeys after infection with *P. knowlesi*, which produced an overwhelming infection, with 50 per cent. of red cells parasitized. The red cells were then washed free from serum and preserved by freezing and drying in 5 cc. amounts. The stored antigen was rehydrated and diluted 1 : 100 in normal saline, which is well beyond the anti-complementary range and is highly antigenic. Tests were then set up as for the Wassermann reaction. It was found that serum of patients with *vivax* and *falciparum* malaria would fix complement with the monkey parasite antigen in approximately the same dilutions as serum from patients with *P. knowlesi* malaria (used in the treatment of general paresis).

The antigen is capable of reacting with heterologous as well as with homologous malaria sera. Sera with positive Wassermann reaction were negative in the absence of malaria, and positive only when malaria infection was present. Control sera from patients with other infectious diseases, and from animals with trypanosomiasis and piroplasmosis gave negative tests. The usefulness of this test in diagnosis depends on its being positive when it is not possible to detect parasites in stained thick or thin blood smears.

Serum was obtained from 12 patients with general paresis inoculated with *P. vivax*. They were then bled at 10-day intervals and blood was examined for parasites. When the parasites could no longer be found serum was obtained until the complement-fixation test became negative. Complement-fixing antibodies appeared in the serum before the peak of the malarial infection, or about two weeks after the onset of clinical symptoms, and persisted for five months after the disappearance of circulating parasites. More practical tests with naturally acquired malaria in the field are obviously indicated. *P. Manson-Bahr.*

Dulaney (Anna Dean), Stratman-Thomas (Warren K.) & Warr (Otis S.). **Complement Fixation in Malaria with Special Reference to the Diagnosis of Naturally Acquired Infections.**—*Jl. Bacteriology.* 1941. Jan. Vol. 41. No. 1. p. 66.

" Earlier studies of complement fixation in induced malaria indicated that this reaction might be successfully used in the diagnosis of naturally acquired infections. Accordingly, 311 patients whose histories and symptoms suggested malaria were tested, and the results of complement fixation compared with blood-smear findings. For all of the tests we used the concentrated *Plasmodium knowlesi* antigen previously described.

" Of the 311 patients, 117 had positive blood smears and 90 gave positive complement-fixation tests. Twenty-eight of the 90 had received some antimalarial drug. Of this group, 76 were infected with *Plasmodium vivax* and 14 with *Plasmodium falciparum*. Twenty-seven patients with positive blood smears (18 were *Plasmodium vivax* ; 9 *Plasmodium falciparum*) gave negative complement-fixation tests. Of this group, 17 had received antimalarial drugs. No parasites were found in blood smears from 194 of the 311 patients. Negative complement-fixation tests were given by 173. Of these, eight had had parasites in the blood, but had completed treatment. Twenty-one of the 194 gave positive complement-fixation tests. Five had received treatment. As controls, the sera from 267 patients with bacterial or protozoan infections and 91 presumably normal individuals were tested. Thirty-one positive complement-fixation tests were obtained.

" Approximately 80 per cent. of the patients with naturally acquired malaria yielded positive complement-fixation tests at a time when parasites were present in the blood. A negative test did not exclude malaria, for parasites were demonstrated in blood smears at such a time. The complement-fixation reaction remained positive for 2 months or longer after the disappearance of parasites from the blood."

Eagle (Harry), Mays (J. R. S.), Hogan (R. B.) & Burney (L. E.). **The Reactivity of the Serum of Malarial Patients with Spirochetal Suspensions.**—*Amer. Jl. Syph.* 1941. July. Vol. 25. No. 4. pp. 406–411.

Malarial infections may yield positive Wassermann and flocculation tests in the absence of syphilitic infection. A complement fixation test, using cultured spirochaetes as antigen is a specific and sensitive test for syphilis. Observations here described, were carried out to determine whether the spirochaete complement fixation test could serve to differentiate syphilitic from malarial infections.

Eleven patients who presented no clinical or serological evidence of syphilitic infection were inoculated with tertian malaria. At irregular intervals before and after inoculation blood specimens were collected. Six uninoculated patients, three syphilitic and three normal, served as controls. Each serum was tested with a complement fixation test, using a washed suspension of cultured spirochaetes (Reiter and Kazan strain) as antigen; with an Eagle micro-flocculation test; and a Wassermann test (Eagle modification). Most of the positively reacting sera were titred. The spirochaetal complement fixation test actually gave a larger proportion of positive and doubtful reactions in the malarial patients than did either the Wassermann or flocculation tests. In 127 specimens collected after the malaria inoculations the Wassermann test was positive in 7 and doubtful in 5: the flocculation test was positive in 11 and doubtful in 6: the spirochaetal test was positive in 19 and doubtful in 16. The spirochaetal complement fixation test does not permit the serological differentiation of syphilis and malaria. It may be that the serologically active substances which appear during malaria infections cross-react with cultured spirochaetes more strongly than they do with tissue lipoids. *N. W.*

Asai (Masaaki). Zum Studium der Serodiagnostik der Malaria. II. Mitt. Ueber die Kongorot-Flokkulation nach Oda-Asai. [**Serological Diagnosis of Malaria: Congo Red Flocculation: the Oda-Asai Test.**]—*Taiwan Igakkai Zassi* (*Jl. Med. Assoc. Formosa*). 1941. Jan. Vol. 40. No. 1. [In Japanese pp. 45–54. With 2 charts. [10 refs.] German summary pp. 55–56.]

It is known that colloidal dyes, such as Congo red, flocculate in solutions of salts, such as quinine hydrochloride, of certain strengths, and that this flocculation is inhibited in the presence of albumin and increased in the presence of globulin. To 5 cc. of a mixture of 0·1 per cent. Congo red solution (5 cc.) and 0·5 cc. serum to be tested, are added 5 cc. of 0·3 per cent. solution of quinine hydrochloride. This is well shaken. After 1–2 hours at room temperature the mixture is centrifuged and the supernatant fluid is compared in a colorimeter (Authenrieth) with a four times diluted 0·1 per cent. Congo red solution. The stronger the flocculation the more transparent the fluid, and the more can the colorimeter scale be read. The test becomes positive within 4 days of infection; it was positive in 19 of 21 acute cases, with a mean scale value of 60·8, in 19 of 24 latent cases, value 82·4, in 49 of 54 chronic cases, value 66·4. After treatment the proportion of positives falls but the scale values rise.

Positive results are also given in tuberculosis, kala azar, liver diseases, syphilis, typhoid and pneumonia. *C. W.*

Bardhan (P. N.). **Effect of Administration of Quinine on the Finding of Malarial Parasites in the Peripheral Blood.**—*Calcutta Med. Jl.* 1941. Mar. Vol. 38. No. 3. pp. 125–126. With 1 chart.

Two cases are reported in which malaria parasites (*P. vivax* in the one, and *P. vivax* with *P. falciparum* in the other) were found after the patients had taken 120 grains and 70 grains of quinine respectively. The first patient was a British soldier whose rise of temperature was continuous, for the first few days, without demonstrable parasites in the blood. This fever is ascribed by the author to coryza [but is quite

characteristic of a primary malarial infection]. The second patient was a child; parasites were found for nine days, during which 70 grains of quinine were given. *C. W.*

Tanaka (Shigeo). Ueber die klinischen Befunde und die Nachkur bei den Malaria-Bestandenen unter den Marinern. [**Clinical Findings after Treatment in Malaria.**]—*Taiwan Igakkai Zassi (Jl. Med. Assoc. Formosa.* 1941. Jan. Vol. 40. No. 1. [In Japanese pp. 13–37. [33 refs.] German summary pp. 37–38.]

The author observed the results of quinine treatment in 79 sailors. The Henry reaction was positive in 50 per cent. within two months of cure but after that in only 13 per cent. Anaemia cleared up usually within a month; the sedimentation rate was normal in about three months. In 9 per cent. basophil cells were seen in the blood. Urobilin was found in the urine in 6 cases, sugar in 6 and albumin in one [but at what period is not stated]. In the group in which infection was due to *P. falciparum* were found:—one case with leucopenia, 3 with microcytosis and anisocytosis, 2 with excess of plasma cells and 5 with urobilinuria. *C. W.*

Napier (L. Everard) & Chaudhuri (R. N.). **A Note on the Treatment of Relapsing Malaria.**—*Indian Med. Gaz.* 1941. June. Vol. 76. No. 6. pp. 335–336.

The authors report a case of benign tertian malaria, with enlargement of the spleen, in which relapses had persistently occurrred in spite of treatment with quinine, atebrin and plasmoquine. The patient, a European, was therefore treated by them as follows:—sod. bicarb., gr. 15, and sod. cit. gr. 30 were given, followed, half an hour later, by 10 grains of quinine, three times a day. Plasmoquine 0·01 gm. twice a day was given concurrently. This was continued for 10 days. On the 11th and 18th days he was given intrasmuscular injections of 18 and 24 cgm. sulpharsenol respectively, and from the 11th day a tonic mixture containing liq. arsenicalis m.4 twice each day. Thereafter he was given a second course of quinine for one week, followed by 30 cgm. sulpharsenol. He remained free of fever for more than six months and gained about 20 lb. in weight.

The points to be noted are the use of quinine with alkali, as advised by Sinton, the addition of plasmoquine, and the use of an arsphenamine preparation (a common practice in the Balkans). These measures are more effective than prolonged use or injection of quinine.

C. W.

Winckel (C. W. F.). **Neoarsphenamine to manage Course of Fever in Therapeutic Malaria.**—*Jl. Amer. Med. Assoc.* 1941. June 14. Vol. 116. No. 24. pp. 2660–2663. With 5 charts.

In the Netherlands neoarsphenamine is used with great success to control the fever in therapeutic malaria. The drug is effective only in *P. vivax* infections. Since 1933 a Madagascar strain of *P. vivax* has been used: local Dutch strains were employed before that date. Infection is conveyed either by the inoculation of infected blood or by mosquito bite. *P. malariae* is also used in therapeutic malaria. Neoarsphenamine has no effect on the fever caused by *P. malariae* infections.

Neoarsphenamine cannot replace quinine in the treatment of malaria but it can effect a considerable reduction in the number of parasites in the peripheral blood and thus suppress benign tertian fever. Different strains of *P. vivax* vary with regard to their sensitivity to neoarsphenamine. The effects of the drug are clearly shown in the five temperature charts that illustrate the paper.

In infections with Dutch strains of *P. vivax* an intravenous injection of 0·15 gm. of neoarsphenamine given after an attack of fever is generally sufficient to convert a quotidian fever to a simple tertian fever. The injection of a similar amount on an afebrile day is generally sufficient to secure freedom from fever for a few days. A series of injections (0·3, 0·45 and 0·6 gm.) cuts short the fever therapy.

The Madagascar strain is more sensitive to neoarsphenamine : a dose of 0·075 gm. is nearly always sufficient to convert a quotidian to a simple tertian fever. A dose of 0·1 gm. is sufficient to obtain a few days' complete remission from fever. *N. W.*

CLARK (Herbert C.). **Review of Recent Research on Drug Prophylaxis and Treatment of Malaria.**—*Southern Med. Jl.* 1941. July. Vol. 34. No. 7 pp. 703–708. [25 refs.]

JETTMAR (H. M.). **The Use of Pyrethrum Powder in Colloidal Solution as Larvicide.**—*Chinese Med. Jl.* 1941. June. Vol. 59. No. 6. pp. 565–569.

Powdered pyrethrum scattered over water in a proportion of 50–100 gm. per 1,000 litres kills with certainty all culicine and anopheline larvae, provided these do not escape from its action. It is therefore recommended for water tanks or small collections of stagnant water. During the cold season (25°C.) anopheline larvae paralysed by fatal dilutions of pyrethrum for hours may recover entirely if transferred to clean water. This does not happen during the hot season (25–30°C.)

V. B. Wigglesworth.

JORDAN (J. H.) & SILVEY (W. J.). **The Comparative Value of Phenothiazine, Paradichlorbenzene, Tetralin, Trichlorethylene and Pyrethrum Extracts as Mosquito Larvicides.**—*Chinese Med. Jl.* 1941. July. Vol. 60. No. 1. pp. 66–72.

The authors consider that a pyrethrum-containing larvicide (that is, an emulsion in soap and water of a light oil containing pyrethrum extract), the results of which are observable within a few hours, is best suited to local conditions in Shanghai. But limitations in the supply of pyrethrum extracts and their increasing cost have led them to seek for economical substitutes. The four substances mentioned in the title were selected for testing. Paradichlorbenzene is a stable addition to pyrethrum larvicides permitting reduction in the quantity of pyrethrum used. Used alone it is the best substitute for pyrethrum but is difficult to dissolve in bulk. Tetralin (tetrahydronaphthalene) is likewise a useful addition ; dearer than the paradichlorbenzene and pyrethrum, but much cheaper than the pyrethrum extract. A suitable solvent for phenothiazine (thiodiphenylamine) has yet to be found ; and trichlorethylene proved toxic to fish and birds. *V. B. Wigglesworth.*

KNOWLES (Frederick L.), PARKER (Wiley V.) & JOHNSON (H. A.). **Observations on the Use of "Phenol" Larvicides for Mosquito Control.**—*Public Health Rep.* 1941. Aug. 15. Vol. 56. No. 33. pp. 1637–1641.

"Phenol" larvicides are commercial preparations consisting of cresylic acid in sulphonated oil. It is generally claimed that if they are diluted with water 1 in 30 and applied as a very fine spray the larvicide will remain on the surface of the water long enough to kill mosquito larvae. The authors have tested the material in the laboratory and in the field against anopheline and culicine larvae. It was not found to be nearly as effective as kerosene. For example, in one field experiment mortality after phenol larvicide was estimated at 25–50 per cent.; after kerosene at 98 per cent. In addition, the phenol larvicide is harmful to fish. In the laboratory, applied at the rate of 50 gallons per acre, it killed 100 per cent. of goldfish but only 16 per cent. of culicine larvae. They conclude that it "does not appear to be a desirable larvicide for general mosquito control."

V. B. Wigglesworth.

MISSIROLI (A.). Ueber die Entwicklung der Malaria-parasiten. [**Development of Malaria Parasites.**]—*Zent. f. Bakt.* I. Abt. Orig. 1941. Mar. 15. Vol. 146. No. 8. pp. 353–359. With 3 plates (2 coloured) & 2 figs.

This paper is an amplification of one already reviewed [this *Bulletin*, 1940, Vol. 37, p. 671]. The author claims to have shown that sporozoites injected do not undergo development at the site of inoculation, or at least if any change takes place in them in this situation it is of no importance from the point of view of producing an infection. In support of this it is stated that if sporozoites are injected under the skin of the wing near its tip and the wing is amputated at the proximal joint within five minutes of the injection no infection will follow. If, however, five minutes are allowed to elapse before amputation, infection will occur, thus proving that sporozoites had already made their way from the tip of the wing to the internal organs. It is concluded that this migration takes place along the lymphatics and that it is within them that the extracellular development with four-nucleated schizonts occurs. This development, which has been followed in smears of the organs, occupies from 12–30 hours and the four resulting merozoites in the case of certain species of *Plasmodium* enter red blood corpuscles only, while in the case of other species red blood corpuscles and tissue cells are both invaded. The author notes that his observations are in disagreement with those of KIKUTH and MUDROW [this *Bulletin*, 1940, Vol. 37, p. 671], who maintain that the sporozoites undergo development within endothelial cells. The paper is illustrated by two coloured plates and one plate of microphotographs. The coloured plates show clearly the stages described, but it is not always evident that the parasites depicted are extracellular, for in smears of liver and spleen the limits of the cell cytoplasm are often difficult to make out, while smear-making may easily damage cells so that parasites which are definitely intracellular may give the impression of being outside the cells.

C. M. W.

HUFF (Clay G.). **Comparisons of a Clon of *Plasmodium cathemerium* with its Parent Strain and with Two Strains derived from the Clon by Mosquito Transmission.**—*Jl. Infect. Dis.* 1941. Mar.–Apr. Vol. 68. No. 2. pp. 184–187.

From a strain of *Plasmodium cathemerium* in canaries a clon was produced by isolation of a single parasite. From this clon two other clons were obtained by mosquito transmission after the 25th and 30th passages. The parent strain and the three clons were studied from the points of view of the size and variability of the oöcysts produced in *Culex pipiens*, the average number of oöcysts per mosquito and the infectivity to mosquitoes. The production of the clon by isolation of a single parasite reduced the variability of the oöcysts, but this variability was not restored by the two mosquito transmissions. The three clons, as regards average size of oöcysts or number of oöcysts per mosquito, did not differ from the parent strain. One of the strains through direct passage from bird to bird had lost very largely its power to produce gametocytes. That some were present was proved by infections developed in mosquitoes. The power to produce gametocytes in large number was restored by mosquito transmission.

[A clon or clone is defined as a group of individuals of like hereditary constitution, traceable through asexual reproduction to a single ancestral zygote.] *C. M. W.*

HEGNER (Robert), WEST (Evaline), RAY (Mary) & DOBLER (Marian). **A New Drug Effective against Bird Malaria.**—*Amer. Jl. Hyg.* 1941. May. Vol. 33. No. 3. Sect. C. pp. 101–111. With 9 figs.

During the course of investigations directed to the discovery of a drug more effective than quinine hydrochloride, in the treatment of malaria in birds, it was found that the quinine derivative hydroxyethylapocupreine was equal in action to quinine hydrochloride on three species of bird malarial parasite. It had, moreover, the advantage of being less toxic, so that considerably larger doses could be given. The authors express the view that as malarial parasites of birds react to drugs similarly to those of man, it would seem probable that the derivative under discussion will prove to be effective against human malaria. *C. M. W.*

RELAPSING FEVER, RAT-BITE FEVER, LEPTOSPIROSIS.

CHEN (Kuo-ching). **Growth of Louse-Borne Relapsing Fever Spirochetes in Chick Embryo.**—*Proc. Soc. Experim. Biol. & Med.* 1941. Apr. Vol. 46. No. 4. pp. 638–639.

"It is well known that important biological differences exist between the tick-borne and louse-borne relapsing fever spirochetes. With the former, infection can readily be produced in a large variety of laboratory animals which together with the tick, serve as means of keeping the strain in the laboratory. On the other hand, few animals were found to be susceptible to the louse-borne type, and the lice cannot be used to maintain the spirochetes."

In this preliminary contribution it is stated that blood was taken from seven patients with louse-borne relapsing fever in Peiping and inoculated into the yolk sac or beneath the chorio-allantoid membrane of hens' eggs; the shells were then sealed. Good growth of spirochaetes was seen in the blood of the embryos, rising to a maximum on the fifth day. The number of organisms was greatly increased after three passages; growth depends on the living embryo, the spirochaetes soon disappearing after death has occurred. *C. W.*

DAVIS (Gordon E.). *Ornithodoros turicata*: **the Male; Feeding and Copulation Habits, Fertility, Span of Life, and the Transmission of Relapsing Fever Spirochetes.**—*Public Health Rep.* 1941. Sept. 5. Vol. 56. No. 36. pp. 1799–1802.

"1. Twelve male *O. turicata* were observed for feeding and copulation habits, the transmission of relapsing fever spirochaetes, span of life, and for fertility as 'old' males in comparison with young males.

"2. Based on 100 observations, time for complete engorgement varied from 6 to 23 minutes.

"3. Based on 100 observations, the time required to complete the act of mating varied from 12 to 60 minutes, with the majority falling between 21 and 35 minutes.

"4. The male may transmit spirochetes at each feeding throughout life; it may transmit them irregularly or, after several successive transmissions, it may fail to effect further transmissions.

"5. A comparison of the fertility of virgin males and 'old' males suggests that mating of the latter results in a larger proportion of fertile eggs.

"6. Test feedings of 6 females (a total of 22 feedings) after each mating with spirochete-carrying males and 1,229 test feedings of the progeny of these matings failed to infect white mice.

"7. The span of adult male life under laboratory conditions varied from 15 to over 36 months."

HAWKING (Frank). **Relapsing Fever: Cerebrospinal Fluid and Therapy.**—*Jl. Trop. Med. & Hyg.* 1941. Aug. 15. Vol. 44. No. 16. pp. 104–105.

The author has examined the cerebrospinal fluid of 12 cases of East African relapsing fever (*S. duttoni*) at Kahama in the Central Province of Tanganyika, in which region the disease is endemic and the native huts swarm with *Ornithodorus moubata*. In each case lumbar puncture was performed and the search for spirochaetes made by injecting 0·5 to 1 cc. of c.s.f. intraperitoneally into each of two mice. Parasites were never found by direct examination, but 5 out of the 12 fluids produced infection in mice. Three of the patients showed clinical and pathological signs of meningitis, but in the other two there was no evidence that the meninges were specifically affected.

The results of treatment are difficult to evaluate, but Arsant (a compound of the Salvarsan type in which one of the two arsenic atoms is replaced by antimony) was found to have about the same therapeutic potency as neoarsphenamine, and Bayer 205 was found to be ineffective. *E. Hindle.*

CHEN (Y. P.) & ANDERSON (Hamilton H.). **Course and Chemotherapy of Experimental Relapsing Fever in the Chinese Hamster** (*Cricetulus griseus*).—*Proc. Soc. Experim. Biol. & Med.* 1941. Apr. Vol. 46. No. 4. pp. 658–662. With 1 fig. [12 refs.]

The authors find that the Chinese hamster, *Cricetulus griseus*, is very susceptible to infection with a Californian strain of spirochaete transmitted by *Ornithodorus hermsi*, Wheeler. [See this *Bulletin*, 1939, Vol. 36, p. 758.]

In 53 hamsters inoculated intraperitoneally with spirochaetes from infected hamsters the incubation period varied from 24 to 72 hours, and three relapses usually occurred. More than half died in nine to 30 days, generally after two weeks. When blood from infected mice was used, the spirochaetes appeared in 24 to 48 hours, and there were three or four attacks each of four to six days' duration with intervals usually of 24 hours. Although the infections were longer, fatalities were less frequent, but about one-fifth died in 12 to 37 days. Brains of untreated animals, removed eight to ten days after the blood was negative, showed spirochaetes in sections stained by Steiner's method.

A study of the chemotherapy of this strain of relapsing fever in Chinese hamsters was attempted using neoarsphenamine and a less toxic arsenical known as Trisodarsen, the tri-sodium salt of 4,4[1] dihydroxy-arsenobenzene-N,N[1] dimethylene sulphonic acid. Thirty hamsters were infected with mouse blood and 30 with blood from other hamsters. Half of each group was then treated with one drug and half with the other, using in each case $\frac{1}{5}$ of LD_{50} (the dose which kills 50 per cent. of the test animals). Of those infected with mouse blood, seven out of 15 treated with neoarsphenamine were still positive 46 hours after the second injection, and $\frac{1}{5}$ of the LD_{50} dose had to be given before all the animals had negative blood smears. Four developed residual infections and two out of 15 died. Of those infected with hamster blood, all appeared negative 46 hours after the second injection, but five showed residual infections, and three out of the 15 died within nine days.

Hamsters infected with mouse blood responded promptly to treatment with trisodarsen and all appeared negative within 46 hours of the second injection, but there were three residual infections and two out of the 15 animals died. Hamsters infected with hamster blood also all became negative after the second injection, and none of them showed any residual infection. Two of the 15 died within 19 days.

Eight out of 15 untreated hamsters showed residual infections. It would seem, therefore, that both drugs possess well marked spirochaeticidal properties, trisodarsen giving rather more satisfactory results than neoarsphenamine. *E. H.*

ISHII (Nobutaro), SHIMIZU (Shigeya) & TSUDA (Kyosuke). **The Effect of Sulfapyridine on Experimental Spirochaetosis Recurrentis.**—*Japanese Jl. Experim. Med.* 1941. Feb.–June. Vol. 19. Nos. 1–3. pp. 5–9.

" 1. The experimental investigations on the therapeutic value for spirochaetae (Treponema duttoni) of several medicaments, such as Sulfapyridine, Sulfa-methyl-thiazol, Prontosil album, Diseptal A, and Sulfanilanilide, were carried out. And it was proved that Sulfapyridine possessed an effective power against spirochaetae.

"2. The therapeutic value of Sulfapyridine on spirochaetae was compared with that of Osvarsan (arsenic compound). The former showed a sufficiently effective power in a dose of 0·01 g. (1 : 100), while the latter in a dose of 0·002 g. (1 : 500). Consequently the therapeutic value of Osvarsan was five times as much as that of Sulfapyridine.

"3. The dose of Sulfapyridine for a patient is usually 3·0–5·0 g. and that of Osvarsan 0·75 g.; therefore the dose of the former is 4–6·6 times as much as that of the latter. It is clear that the same therapeutic results for spirochaetae may be practically obtained by these two medicaments."

HUART. Rattenbeetziekte. [**Rat-Bite Fever.**] [Verslagen der Afdeelingsvergaderingen, Military Hospital, Batavia, 1940, Dec. 19.]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1941. Apr. 22. Vol. 81. No. 16. pp. 900–903.

The patient was a soldier of Amboina who came to hospital with fever, 39·8°C., diarrhoea, enlarged spleen, a tongue furred with red edge, short of breath and cyanotic. A preliminary diagnosis of typhoid fever was made, but repeated trials of agglutination tests with the enteric group, and also Brucella and Leptospirae gave uniformly negative results. It was then found that a month before he had been bitten on his right middle finger by a rat. There still remained a slight purple-red stain and perhaps a little swelling and an axillary gland was enlarged. Improvement was rapid and complete after an injection of 300 mgm. of neosalvarsan. *H. H. S.*

GREENGARD (Joseph) & HESS (Edmond R.). **Rat-Bite Fever in an Infant Bitten at the Age of Eleven Days.**—*Jl. Amer. Med. Assoc.* 1941. May 24. Vol. 116. No. 21. pp. 2393–2394.

The description of a typical and fatal case of rat-bite fever in an infant negress aged 11 days. The patient was brought to hospital about two hours after having been bitten in the hand by a rat. The wound healed quickly, but after an incubation period of 12 days, symptoms of rat-bite fever developed and the infant died one month later. An intercurrent infection of the respiratory tract developed two weeks after the onset of rat-bite fever. The specific organism was recovered by inoculation into mice of blood collected from the patient during the first febrile attack.

The authors give clinical details of the case, which seems to be the youngest hitherto reported. *E. H.*

STEFANOPOULO (G.-J.) & CHEVÉ (J.). Culture de *Leptospira icterohemorragiae* en tissus embryonnaires de poulet. [**The Culture of *Leptospira icterohaemorrhagiae* in Fowl Embryonic Tissue.**]—*Bull. Soc. Path. Exot.* 1940. Vol. 34. Nos. 1–3. pp. 15–17. With 1 fig.

The authors confirm the observation by MORROW, SYVERTON, STILES and BERRY [see this *Bulletin*, 1939, Vol. 36, p. 772] that *L. icterohaemorrhagiae* can be grown on the chorio-allantoic membrane of the fowl embryo, and reproduce a microphotograph of a section of the liver of an infected embryo, showing the very large number of spirochaetes present in this organ.

Attempts were made to culture the organism, *in vitro*, in a medium containing embryonic tissue, and the following method was found to give the best results :—

In each sterile test tube is run in 10 cc. of a filtered extract of clotted horse blood, and 0·2 cc. of a suspension of the brain of a 12- to 15-day fowl embryo. The medium is then covered with a layer of sterile oil or vaseline and incubated 24–48 hours in order to check sterility. The extract of clotted horse blood may be replaced by Tyrode solution and the brain by other tissues of the fowl embryo.

The medium will keep for at least one month if kept in the dark at room temperature. When required for use each tube is inoculated with the material to be tested and incubated at 29°C. for four to five days, after which cultures can be kept at room temperature. The authors have obtained five successive passages without the agglutination properties of the strain showing any alteration. *E. H.*

SMITH (J.). **The Treatment of Weil's Disease.**—*Med. Press & Circular.* 1941. July 23. Vol. 206. No. 4. pp. 87–89. [14 refs.]

The author describes briefly the clinical features of the disease, making special reference to meningitis, which was found to occur as a complication in 10 per cent. of a series of cases recently seen in Aberdeen. This meningitis is mild in character and appears to have little prognostic value. The age of the patient, however, is of great importance, and the case mortality rate in those over 50 is immensely greater than in younger people. The absence of jaundice is a sign of good prognosis. During the febrile stage leptospirae can be found in the blood in almost every case, but from the sixth or seventh day agglutinins and lysins are found in rising titre and the organisms disappear. In the second and third weeks leptospirae may be recovered from the urine.

Treatment may be discussed under three headings : symptomatic treatment, chemotherapy and serum therapy. Symptomatic treatment consists of the administration of diaphoretics, a diet rich in carbohydrate and poor in protein and fat, and plenty of fluid. Chemotherapy with bismuth preparations is effective in animals but has not been attempted in man ; there is no evidence that the sulphonamides exert any beneficial effect. Serum (prepared in Britain against *L. icterohaemorrhagiae*) should be given early, before damage has been done to the kidneys or liver ; 30 to 60 cc. may be injected intramuscularly or intravenously, and repeated if necessary. Little benefit may be expected from the administration of serum after the sixth day, but when given at an early stage the effect is immediate. Serum may be used as a prophylactic agent in those who have been exposed to infection.

C. W.

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